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[Diagnostic Test Accuracy Review]

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection

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ABSTRACT

Background

Sample collection is a key driver of accuracy in the diagnosis of SARS-CoV-2 infection. Viral load may vary at different anatomical sampling sites and accuracy may be compromised by difficulties obtaining specimens and the expertise of the person taking the sample. It is important to optimise sampling accuracy within cost, safety and accessibility constraints.

Objectives

To compare the sensitivity of different sampling collection sites and methods for the detection of current SARS-CoV-2 infection with any molecular or antigen-based test.

Search methods

Electronic searches of the Cochrane COVID-19 Study Register and the COVID-19 Living Evidence Database from the University of Bern (which includes daily updates from PubMed and Embase and preprints from medRxiv and bioRxiv) were undertaken on 22 February 2022. We included independent evaluations from national reference laboratories, FIND and the Diagnostics Global Health website. We did not apply language restrictions.

Selection criteria

We included studies of symptomatic or asymptomatic people with suspected SARS-CoV-2 infection undergoing testing. We included studies of any design that compared results from different sample types (anatomical location, operator, collection device) collected from the same participant within a 24-hour period.

Data collection and analysis

Within a sample pair, we defined a reference sample and an index sample collected from the same participant within the same clinical encounter (within 24 hours). Where the sample comparison was different anatomical sites, the reference standard was defined as a nasopharyngeal or combined naso/oropharyngeal sample collected into the same sample container and the index sample as the alternative anatomical site. Where the sample comparison was concerned with differences in the sample collection method from the same site, we defined the reference sample as that closest to standard practice for that sample type. Where the sample pair comparison was concerned with differences in personnel collecting the sample, the more skilled or experienced operator was considered the reference sample.

Two review authors independently assessed the risk of bias and applicability concerns using the QUADAS-2 and QUADAS-C checklists, tailored to this review.

We present estimates of the difference in the sensitivity (reference sample (%) minus index sample sensitivity (%)) in a pair and as an average across studies for each index sampling method using forest plots and tables. We examined heterogeneity between studies according to population (age, symptom status) and index sample (time post-symptom onset, operator expertise, use of transport medium) characteristics.

Main results

This review includes 106 studies reporting 154 evaluations and 60,523 sample pair comparisons, of which 11,045 had SARS-CoV-2 infection. Ninety evaluations were of saliva samples, 37 nasal, seven oropharyngeal, six gargle, six oral and four combined nasal/oropharyngeal samples. Four evaluations were of the effect of operator expertise on the accuracy of three different sample types. The majority of included evaluations (146) used molecular tests, of which 140 used RT-PCR (reverse transcription polymerase chain reaction). Eight evaluations were of nasal samples used with Ag-RDTs (rapid antigen tests). The majority of studies were conducted in Europe (35/106, 33%) or the USA (27%) and conducted in dedicated COVID-19 testing clinics or in ambulatory hospital settings (53%). Targeted screening or contact tracing accounted for only 4% of evaluations. Where reported, the majority of evaluations were of adults (91/154, 59%), 28 (18%) were in mixed populations with only seven (4%) in children. The median prevalence of confirmed SARS-CoV-2 was 23% (interquartile (IQR) 13%-40%).

Risk of bias and applicability assessment were hampered by poor reporting in 77% and 65% of included studies, respectively. Risk of bias was low across all domains in only 3% of evaluations due to inappropriate inclusion or exclusion criteria, unclear recruitment, lack of blinding, nonrandomised sampling order or differences in testing kit within a sample pair.

Sixty-eight percent of evaluation cohorts were judged as being at high or unclear applicability concern either due to inflation of the prevalence of SARS-CoV-2 infection in study populations by selectively including individuals with confirmed PCR-positive samples or because there was insufficient detail to allow replication of sample collection.

When used with RT-PCR

- There was no evidence of a difference in sensitivity between gargle and nasopharyngeal samples (on average -1 percentage points, 95% CI -5 to +2, based on 6 evaluations, 2138 sample pairs, of which 389 had SARS-CoV-2).
- There was no evidence of a difference in sensitivity between saliva collection from the deep throat and nasopharyngeal samples (on average +10 percentage points, 95% CI -1 to +21, based on 2192 sample pairs, of which 730 had SARS-CoV-2).
- There was evidence that saliva collection using spitting, drooling or salivating was on average -12 percentage points less sensitive (95% CI -16 to -8, based on 27,253 sample pairs, of which 4636 had SARS-CoV-2) compared to nasopharyngeal samples. We did not find any evidence of a difference in the sensitivity of saliva collected using spitting, drooling or salivating (sensitivity difference: range from -13 percentage points (spit) to -21 percentage points (salivate)).
- Nasal samples (anterior and mid-turbinate collection combined) were, on average, 12 percentage points less sensitive compared to nasopharyngeal samples (95% CI -17 to -7), based on 9291 sample pairs, of which 1485 had SARS-CoV-2. We did not find any evidence of a difference in sensitivity between nasal samples collected from the mid-turbinates (3942 sample pairs) or from the anterior nares (8272 sample pairs).
- There was evidence that oropharyngeal samples were, on average, 17 percentage points less sensitive than nasopharyngeal samples (95% CI -29 to -5), based on seven evaluations, 2522 sample pairs, of which 511 had SARS-CoV-2.

A much smaller volume of evidence was available for combined nasal/oropharyngeal samples and oral samples.

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Age, symptom status and use of transport media do not appear to affect the sensitivity of saliva samples and nasal samples.

When used with Ag-RDTs

- There was no evidence of a difference in sensitivity between nasal samples compared to nasopharyngeal samples (sensitivity, on average, 0 percentage points -0.2 to +0.2, based on 3688 sample pairs, of which 535 had SARS-CoV-2).

Authors' conclusions

When used with RT-PCR, there is no evidence for a difference in sensitivity of self-collected gargle or deep-throat saliva samples compared to nasopharyngeal samples collected by healthcare workers when used with RT-PCR. Use of these alternative, self-collected sample types has the potential to reduce cost and discomfort and improve the safety of sampling by reducing risk of transmission from aerosol spread which occurs as a result of coughing and gagging during the nasopharyngeal or oropharyngeal sample collection procedure. This may, in turn, improve access to and uptake of testing. Other types of saliva, nasal, oral and oropharyngeal samples are, on average, less sensitive compared to healthcare worker-collected nasopharyngeal samples, and it is unlikely that sensitivities of this magnitude would be acceptable for confirmation of SARS-CoV-2 infection with RT-PCR.

When used with Ag-RDTs, there is no evidence of a difference in sensitivity between nasal samples and healthcare worker-collected nasopharyngeal samples for detecting SARS-CoV-2. The implications of this for self-testing are unclear as evaluations did not report whether nasal samples were self-collected or collected by healthcare workers. Further research is needed in asymptomatic individuals, children and in Ag-RDTs, and to investigate the effect of operator expertise on accuracy.

Quality assessment of the evidence base underpinning these conclusions was restricted by poor reporting. There is a need for further high-quality studies, adhering to reporting standards for test accuracy studies.

PLAIN LANGUAGE SUMMARY

How accurate are different types of sample collection for diagnosing COVID-19 infection?

Key messages

- When used with RT-PCR tests (a molecular test that detects genetic material in COVID-19 using a technique called reverse transcription polymerase chain reaction), self-collected gargle and deep throat saliva samples have a similar sensitivity compared to trained healthcare worker-collected nasopharyngeal samples (taken from the back of the throat through the nose) in detecting COVID-19.
- When used with RT-PCR, samples collected from the nose, oropharynx (throat via the mouth), oral cavity, and other saliva collection methods are less sensitive for detecting COVID-19 compared to healthcare worker-collected nasopharyngeal samples.
- When used with rapid antigen tests (Ag-RDTs; at-home/self-tests), samples collected from the nose have a similar sensitivity to healthcare worker-collected nasopharyngeal samples in detecting COVID-19.

Why is improving the diagnosis of COVID-19 important?

Coronavirus disease (COVID-19) is caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). People with suspected COVID-19 may decide to take a test to know whether they are infected, so that they can receive treatment, and follow recommended guidance to self-isolate and inform close contacts. Not detecting COVID-19 when it is present (a false negative result) risks spreading infection and results in missed opportunities for treatment.

Types of sample collection methods for diagnosing COVID-19?

The type and quality of sample taken for confirmation of COVID-19 affects the reliability of diagnosis. The most accurate type of sample to diagnose COVID-19 is that taken by a trained healthcare worker from the back of the throat through the nose (a nasopharyngeal sample). This type of test detects genetic material in the virus using a technique called reverse transcription polymerase chain reaction (RT-PCR). However, this sample is difficult to obtain correctly, causes discomfort and risks spreading infection if individuals cough or sneeze when the sample is taken. Alternative sample types, particularly those that can be self-collected using rapid antigen tests (Ag-RDTs; i.e. self-tests), may reduce cost and discomfort and improve the safety of sampling. This may, in turn, improve access to and uptake of testing.

What did we want to find out?

We wanted to compare the sensitivity of different sample sites and collection methods in detecting COVID-19 with molecular tests (RT-PCR tests) or self-based tests (Ag-RDT tests).

What did we do?

We searched for studies that had compared the accuracy of nasopharyngeal samples to any alternative that could be used in patients outside of hospital, including nose (nasal) samples, throat samples taken through the mouth (oropharyngeal), gargle samples and saliva

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samples. We looked at the use of samples with either RT-PCR or Ag-RDTs. We also searched for studies that had compared different methods for taking samples, such as samples collected by a healthcare worker compared to those collected by individuals with no or minimal instructions.

What did we find?

The review included 106 studies with a total of 60,523 participants, of whom 11,045 had COVID-19 infection. Fifty-nine per cent of studies were conducted on adults and 79% on symptomatic or mixed symptomatic and asymptomatic participants. Sixty per cent of studies took place in Europe or the USA; just over half (55%) took place in dedicated COVID-19 testing centres or in outpatient settings.

Main results

With RT-PCR, on average:

- 100% of positive nasopharyngeal samples collected by healthcare workers would also test positive on self-collected gargle samples or saliva samples (collected by coughing and then spitting (deep throat saliva));
- 88% of positive nasopharyngeal samples collected by healthcare workers would also test positive with self- or healthcare worker-collected nose samples;
- 87% of positive nasopharyngeal samples collected by healthcare workers would also be detected by saliva self-collected using spitting, 84% by saliva self-collected using drooling and 79% by saliva self-collected by sucking on a swab; and
- 83% of positive nasopharyngeal samples collected by healthcare workers would also be detected by self- or healthcare worker-collected oropharyngeal samples.

With Ag-RDTs, on average:

- 100% of positive nasopharyngeal samples collected by healthcare workers would also be detected by self-collected or healthcare worker-collected nose samples.

Summary results

The results of these studies indicate that in a group of 1000 people, of whom 230 (23%) have COVID-19, then:

when used with PCR, compared to healthcare worker-collected nasopharyngeal samples:

- no cases of COVID-19 would be missed using self-collected gargle samples (12 less to 5 more) or deep throat saliva samples (2 less to 48 more);
- 28 (16 to 39) fewer cases of COVID-19 infection would be detected using healthcare worker- or self-collected nose sample;
- 30 (18 to 41) fewer cases of COVID-19 infection would be detected by saliva self-collected using spitting, 37 (12 to 62) fewer by saliva collected by drooling and 48 (12 to 85) fewer by saliva collected by sucking on a swab;
- 39 (12 to 67) fewer cases of COVID-19 infection would be detected by healthcare worker- or self-collected oropharyngeal samples; and

when used with Ag-RDTs, compared to healthcare worker-collected nasopharyngeal samples:

no cases of COVID-19 infection would be missed using healthcare worker- or self-collected nose samples.

What are the limitations of the evidence?

It was often not clear whether included studies deliberately excluded inadequate samples or whether the results of the more accurate nasopharyngeal sample were known when alternative samples were interpreted. This may have resulted in alternative sample types appearing more accurate than they are in practice, decreasing the number of missed cases of COVID-19 infection.

More than half of studies did not give information about how long participants had had symptoms at the time of sampling. This reduces our confidence in the comparison of different sample types.

Most studies evaluated self-collected samples by adults with symptoms for use with RT-PCR; therefore, the findings of this review may not be applicable to asymptomatic individuals or children. For studies conducted with Ag-RDTs, it is unclear whether sensitivity estimates of nose samples are applicable to home use (self-collected and self-interpreted).

How up to date is this review?

The evidence is current to 22 February 2022.

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SUMMARY OF FINDINGS

Summary of findings 1. Sensitivity of different anatomical sample sites for the diagnosis of SARS-CoV-2 infection

Question	What is the diagnostic accuracy of different sample sites and sample collection methods for the diagnosis of SARS-CoV-2 infection?
Population	Symptomatic adults or children with suspected current SARS-CoV-2 infection Adults and children undergoing screening for SARS-CoV-2 infection including: - asymptomatic contacts of confirmed COVID-19 cases; and - community screening
Index tests	We included samples suitable for testing in an ambulatory setting, including upper respiratory, saliva, gargle and oral samples. We included samples acquired and tested by study participants and trained or untrained study personnel (healthcare workers or laboratory scientists), using any collection method, with or without inactivation and stabilisation with transport media.
Target condition	Detection of current SARS-CoV-2 infection
Reference standard	For 2 samples used with molecular or antigen-based tests performed on the same individuals in the same clinical encounter: - for SARS-CoV-2 cases, a positive result on any one sample; - for non-SARS-CoV-2 cases, a negative result on both sample types.
Consequences of test errors	False negative results mean missed cases of SARS-CoV-2 infection, with either delayed or no confirmed diagnosis and increased risk of community transmission due to a false sense of security. False positives were not quantified in this review because we assumed these were negligible: < 1% for molecular tests and 1-2% for rapid antigen tests.

Quantity of evidence	Sample type	Evaluation cohorts	Total sample pairs, median (IQR)	Confirmed SARS-CoV-2, median (IQR)
	Saliva: overall	90	209 (99 to 409)	56.5 (32 to 85)
	Saliva: deep throat	11	95 (51 to 223)	38 (29 to 58)
	Saliva: drool	11	200 (123 to 236)	59 (35 to 99)
	Saliva: salivate	11	273 (147 to 596)	59 (27 to 108)
	Saliva: spit	35	243 (131 to 595)	58 (32 to 94)
	Saliva: swab & drool	1	928	385
	Nasal: overall	37 (8 in rapid antigen tests)	214 (104 to 369)	36 (16 to 73)
	Oropharyngeal	7	182 (146 to 353)	25 (12 to 105)
	Gargle	6	221.5 (23 to 645)	56.5 (9 to 129)

Nasal/oropharyngeal	4	136.5 (71.5 to 279)	31 (20 to 49.5)
Oral swab	4	328.5 (121 to 500.5)	41.5 (29.5 to 99)
Oral rinse	2	119 (98 to 140)	32.5 (30 to 35)

Limitations of the evidence

Risk of bias

We judged 3% of participant/setting cohorts were at low overall risk of bias.

Participants: A majority (115/135 (85%)) of evaluation cohorts were judged as being at unclear or high risk of bias due to inappropriate inclusions (including selectively including individuals with confirmed PCR-positive samples) and exclusions or unclear recruitment methods.

Index tests: A majority (143/154 (93%)) of sample pair comparisons were judged as being at unclear or high risk due to concerns about blinding, the order in which samples being compared were collected, or differences in the testing technology used for each sample in a pairwise comparison.

Flow and Timing: A majority (126/135 (93%)) of evaluation cohorts were judged as being at unclear or high risk due to imbalances in missing data between sample pairs or lack of clarity about the flow of participants through studies.

Concerns about applicability

We judged that 32% of participant/setting cohorts were at low overall applicability concern.

Participants: Approximately half of the evaluation cohorts (71/135; 53%) were judged as being at high or unclear applicability concern. In three evaluation cohorts judged as being at high applicability concern, this was due to possible enrichment of the tested population with confirmed PCR +ve samples.

Index tests: Almost all (152/154 (99%)) sample pair comparisons were judged as being at unclear or low applicability concern, due to insufficient detail about the index or reference sample collection or testing process to allow replication.

FINDINGS	Evaluations (study cohorts)	Sample pairs	SARS-CoV-2 cases	Difference in sensitivity (95% CI) compared to NP or NP/OP swab
MOLECULAR TESTS**				
Saliva: overall	90 (89*)	40,342 (40,016)*	7341	-0.12 (-0.16 to -0.08)
Saliva: deep throat	11	2192	730	0.10 (-0.01 to 0.21)
Saliva: drool	11	2325	683	-0.16 (-0.27 to -0.05)
Saliva: salivate	11 (10)*	7502 (7176)*	801	-0.21 (-0.37 to -0.05)
Saliva: spit	35	17,752	3152	-0.13 (-0.18 to -0.08)
Saliva: swab & drool	1	928	385	-0.01 (-0.04 to 0.02)
Nasal: overall (anterior and mid-turbinate)	29	9291	1485	-0.12 (-0.17 to -0.07)
Oropharyngeal	7	2522	511	-0.17 (-0.29 to -0.05)
Gargle	6	2138	389	-0.01 (-0.05 to 0.02)

Nasal/oropharyngeal	4	701	139	0.07 (0.01 to 0.12)
Oral swab	4	1243	257	-0.33 (-0.62 to -0.05)
Oral rinse	2	238	65	-0.20 (-0.38 to -0.02)
Ag-RDTs				
Nasal: overall: (anterior and mid-turbinate)	8	3688	535	0.00 (-0.002 to 0.002)

Average difference in sensitivity and 95% CI compared to reference (NP or NP/OP) sample with MOLECULAR TESTS and applied to a hypothetical cohort of 1000 patients where 230 patients actually have SARS-CoV-2 infection (prevalence 23%)*****

- There would be *no difference* in the number of cases of SARS-CoV-2 infection detected with gargle samples -2 (-12 to +5) or with saliva samples collected from the deep throat -23 (-2 to +48).
- Using nasal samples collected either from the anterior nares or mid-turbينات, on average, would detect 28 *fewer* (-16 to -39) cases of SARS-CoV-2 infection.
- The number of cases of SARS-CoV-2 detected would be, on average, 30 *fewer* (-18 to -41) with saliva samples collected by spitting, 37 *fewer* (-12 to -62) with drooling and 48 *fewer* (-12 to -85) with salivating.
- Using oropharyngeal samples, 39 *fewer* (-12 to -67) cases of SARS-CoV-2 infection would be detected.

Average difference in sensitivity and 95% CI compared to reference (NP) sample with AG-RDTs and applied to a hypothetical cohort of 1000 patients where 230 patients actually have SARS-CoV-2 infection (prevalence 23%)***

- There would be *no difference* in cases of SARS-CoV-2 infection detected 0 (0 to 0) with **nasal samples collected either from the anterior nares or mid-turbينات**.

Notes to table

*Numbers in brackets are those included in calculating the pooled estimates

**146/154 evaluation cohorts used molecular tests; 140 used RT-PCR, four used isothermal techniques with saliva or nasal samples, two used Transcription-Mediated Amplification (TMA) with saliva samples

***Median prevalence taken from included studies

Abbreviations

Ag: antigen; Ag-RDTs: rapid antigen tests; CI: confidence intervals; COVID-19: coronavirus disease 19; IQR: interquartile range; Nos: not otherwise specified; NP: nasopharyngeal; NP/OP: nasopharyngeal/oropharyngeal/ combined swab; PCR +ve: polymerase chain reaction positive; RT-PCR: reverse transcription polymerase chain reaction; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

BACKGROUND

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of 16 August 2023, there had been 769,774,646 confirmed cases of COVID-19, including 6.96 million deaths reported to the World Health Organisation (WHO; [WHO 2023](#)). The majority of confirmed cases have been reported in Europe (2.8 million), followed by the western Pacific (2.1 million) with 1.9 million in the Americas. SARS-CoV-2 poses important diagnostic evaluation challenges. These include evaluating whether in vitro diagnostic tests can accurately identify and rule out current SARS-CoV-2 infection; whether diagnostic accuracy varies according to participant, test and setting specific factors; and optimisation of diagnostic capability for large-scale testing programmes.

Sample collection is a crucial step in the diagnosis of infectious diseases and a key driver of accuracy ([WHO 2021](#)). Viral load is different at different anatomical sampling sites and varies over the course of infection ([Mallett 2020](#); [Weiss 2020](#); [Wolfel 2020](#)). Adequate collection may be compromised by the level of difficulty obtaining specimens, the experience and training of the person taking the sample and discomfort associated with the sampling procedure itself.

This review synthesises the evidence for the effect of different anatomical sample collection sites and methods on the accuracy of molecular or antigen tests for the detection of SARS-CoV-2.

Nasopharyngeal samples are considered to be the most accurate type of sample for detection of SARS-CoV-2 ([WHO 2021](#)), but adequate samples can be difficult to collect, the procedure is uncomfortable for patients and collection requires the use of personal protective equipment (PPE). Safety concerns, equipment shortages and resource requirements such as the need for training for the purposes of testing on a large scale, have prompted investigation into the accuracy of sampling sites and methods that are safer for patients and healthcare workers and pose fewer logistical and economic barriers to their use. Samples that can be adequately self-collected reduce the risk of infection to healthcare workers and reduce costs associated with sample collection. Avoidance of aerosol-generating procedures (nasopharyngeal and oropharyngeal sampling) reduces the risk of transmission to others and "dry" collection (without the use of transport media) may reduce the complexity and therefore adequacy of sample collection whilst reducing equipment demands and costs ([WHO 2020b](#)).

A further factor that may influence the choice of sample to use when implementing testing on a large scale and particularly to ensure willingness to participate in asymptomatic screening, is the acceptability of different sample types and collection procedures. Individual preferences for sample type may be context-specific depending on ease of collection, speed with which results are obtained (for example, certain sample types may not be available or may perform less well with rapid tests) and discomfort associated with the procedure itself ([Zimba 2021](#)). Some sample types (nasal and saliva) can be self-collected with minimal instruction. Nasal swabs have been shown to cause less discomfort than nasopharyngeal and oropharyngeal swabs ([Frazee 2018](#)). A study examining sampling preferences during screening for SARS-CoV-2 infection in schools demonstrated that 36% of children and their guardians agreeing to testing using saliva samples would have

declined had the requirement been for nasal samples ([McLaughlin 2022](#)).

Target condition being diagnosed

COVID-19 is a disease caused by infection with the SARS-CoV-2 virus. The key target condition for this review is current SARS-CoV-2 infection, either symptomatic (i.e. with COVID-19 disease) or asymptomatic, and detected using any molecular or antigen-based test. We use an imperfect reference standard, where we consider the combined test results for two sample types in a single participant taken in the same clinical encounter as confirmation of diagnosis. A positive result for either sample type is considered to indicate the presence of SARS-CoV-2 infection whilst the absence of a positive test result on both sample types (i.e. both test results, negative) is assumed to indicate the absence of SARS-CoV-2 infection ([Appendix 1](#)). We assume that false positives resulting from low-level reactions during molecular or antigen testing, failures in sampling or laboratory protocols (e.g. mislabelling), or contamination during sampling or processing ([Mayers 2020](#)) will be negligible. Similarly, we assume that the contribution of test positives from past rather than current infection will be minimal. Based on population prevalence surveys where SARS-CoV-2 infections are rare ([ONS 2020](#); [Riley 2020](#)), Dinnes and colleagues assumed an upper bound on the possible false positive rate of RT-PCR of less than 0.077% ([Dinnes 2022](#)). The false positive rate of rapid antigen tests has been estimated to be higher than RT-PCR but still low (1.5%) ([Dinnes 2022](#)).

By contrast, false negative rates for RT-PCR have been estimated to be as high as 20% to 30% in the first week after symptom onset ([Arevalo-Rodriguez 2020](#); [Kucirka 2020](#); [Yang 2020](#)). For antigen-based tests, false negatives have been estimated to be as high as 40% in symptomatic individuals ([Dinnes 2022](#)). This review is concerned with the *difference* in sensitivity caused by variation in the sample site or sample collection process. We assume that the impact of the testing method (molecular or antigen) on observed *differences* in sensitivity between different sample sites and collection methods should be minimal, provided the molecular or antigen testing method is the same (test type, gene targets, test positivity threshold, kit) for each sample in a pair, taken in the same clinical encounter.

Index test(s)

This review is concerned with the effect on accuracy of using different sample types (anatomical site and/or collection method) for the identification of current SARS-CoV-2 infection. We considered respiratory and nonrespiratory samples recommended by one or more of the WHO ([WHO 2019](#)), Centres for Disease Control and Prevention (CDC; [Centres for Disease Control 2021](#)), or European Centre for Disease Prevention and Control ([ECDC 2021](#); [ECDC 2022](#)) that would be considered appropriate for use in ambulatory testing settings. Samples tested with either molecular or antigen-based tests were considered for inclusion, providing a sample pair was tested using the same type of testing technology.

Sample collection is noted to be one of the most critical factors affecting the performance of diagnostic tests on respiratory fluids ([WHO 2021](#)). For confirmatory testing with RT-PCR for patients meeting the case definition for suspected SARS-CoV-2, WHO recommends collecting nasopharyngeal and oropharyngeal samples in viral transport media (VTM), combined in the same

tube to increase viral load (WHO 2020a). The CDC recommends collection of an upper respiratory tract (URT) specimen in VTM for confirmatory testing with Nucleic Acid Amplification Tests (NAATs). Saliva is described as having "highly variable quality" for confirmatory SARS-CoV-2 testing with NAATs (Centres for Disease Control 2021) but is considered "an acceptable specimen type" for RT-PCR testing when nasopharyngeal swabs cannot be collected in symptomatic patients or for repeated screening of asymptomatic individuals (Centres for Disease Control 2021). The European Centre for Disease prevention and Control (ECDC) recommend upper respiratory tract (URT) swabs, aspirates or wash as the optimal sample types for detection of current infection with SARS-CoV-2, with saliva being noted as an "alternative specimen" to be used with assays detecting SARS-CoV-2 RNA only (ECDC 2022). For rapid antigen detection tests (Ag-RDT), it is noted that evidence of clinical performance is largely based on nasal, oropharyngeal or nasopharyngeal specimens. CDC and ECDC do not recommend use of saliva with Ag-RDT tests, whilst WHO note that performance is better with URT compared to other sample types (throat wash and saliva) (Brummer 2021; Centres for Disease Control 2021; ECDC 2022; WHO 2021).

We also included sample types not currently recommended, but that might be considered appropriate for ambulatory testing settings, such as swabs of the oral cavity and gargle samples. Samples could be acquired using any method, with or without inactivation and stabilisation with transport media, and collected and tested by study participants, trained or untrained study personnel, or professionals such as healthcare workers or laboratory scientists (Centres for Disease Control 2021).

Anatomical sample site

The main anatomical sites of viral infection may differ so that, for example, in some individuals, SARS-CoV-2 is more readily detected in saliva and in others the nasopharynx. Such differences might also be related to genomic variations between patients (Ghafouri-Fard 2020). The presence of virus at different anatomical sampling sites is also known to vary during the course of infection. Viral RNA levels in symptomatic infection have been shown to peak in the oropharynx and nasopharynx between four and six days post-symptom onset (Wolfel 2020) (about a week earlier than in the lower respiratory tract (LRT)) and remain detectable for a median duration of 12 to 18 days, longer with increasing disease severity (Weiss 2020; Wolfel 2020). Viral load appears to reduce faster in URT compared to LRT samples (Mallett 2020; Weiss 2020), in both mild and more severe infection (Weiss 2020). This pattern of sample positivity is also observed in children, although the duration of viral positivity at each anatomical site is shorter (Weiss 2020). The sensitivity of saliva samples compared to nasopharyngeal samples has been shown to be 100% within the first five days of symptom onset, dropping to 96.4% at 10 days (Uwamino 2021).

Upper Respiratory Tract (URT) samples

The procedure for collecting nasopharyngeal, oropharyngeal and nasal swab samples is standardised and training or supervised instruction is recommended (Centres for Disease Control 2021; ECDC 2022; WHO 2019; WHO 2020a). Nasopharyngeal and oropharyngeal samples and oropharyngeal and nasal samples may be combined in an attempt to improve sensitivity. Nasal swabs can be taken to the depth of the nasal turbinates (nasal mid-turbinate) or from the anterior of the nares (nasal anterior swabs). Some NAAT

tests authorised by the FDA have the capability for self-collection of specimens (Centres for Disease Control 2021). Nasal mid-turbinate and nasal anterior samples also have the advantages of being less invasive compared to nasopharyngeal and oropharyngeal swabs. Nasopharyngeal and nasal (anterior and mid-turbinate) sampling techniques carry a risk of epistaxis, particularly for those with coagulopathy or on anticoagulation therapy (Block-Wheeler 2023; Sri 2020).

Saliva

Saliva is used widely as a diagnostic tool to detect viral infections such as dengue, Ebola, Zika, Yellow fever and recently emerged coronaviruses responsible for severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) (Niedrig 2018). Saliva can be self-collected with minimal training or supervision, and can be collected directly into a sterile container (direct sampling) although dilution may be necessary for viscous samples. Whole saliva is a heterogeneous mixture of saliva secreted in the oral cavity from various glands in addition to other components such as nasal and bronchial secretions, epithelial and immune cells from the oral mucosa and upper airways, food debris, tears, bacteria, and gingival crevicular fluid (Miller 2010). Common collection methods include the passive drooling technique (allowing saliva to pool in the floor of the mouth and drain into a collection tube usually aided by a funnel device), the spitting technique (allowing saliva to pool in the floor of the mouth before spitting into a collection tube) and salivating (asking the patient to stimulate and collect saliva by chewing on a swab placed between the gum and cheek). "Deep throat" or "posterior oropharyngeal" saliva collection includes instruction to clear the throat by coughing or gargling before spitting into a collection device and may in effect combine sputum which is obtained from deep coughing and oral secretions (saliva). The composition of saliva is affected by factors such as the time of day, eating and drinking prior to sample collection and the precise collection method. For example, saliva obtained from spitting contains more bacteria compared to saliva collected using the drooling technique (Bhattarai 2018).

Other sample types included in this review

We did not restrict inclusion of sample types to those currently recommended for use. We considered inclusion of other sample types if they had the potential to be deployed at scale in ambulatory populations. For example, gargling (undertaken by forcing the cricopharyngeal muscle to oscillate over the posterior pharyngeal wall with saline or water) and oral swabs (taken from the dorsal and ventral surfaces of the tongue and the buccal mucosa) are noninvasive and amenable to self-collection (Mane 2022; Tsang 2022). Gargle samples are also swab-free and transport media-free (Tsang 2022).

Sample collection method

In addition to anatomical sites, variations in sample collection methods may affect accuracy. Collection of samples may be undertaken by different "operators"; for example, trained compared to untrained operators and healthcare workers (HCW) compared to self-collected samples. Saliva and nasal samples can be self-collected with minimal instruction and have been demonstrated to have comparable accuracy to samples collected by trained healthcare workers (Tsang 2022). Other elements of the collection process may vary; for example, aspiration or washing

rather than swabbing. Saliva can be collected by a variety of methods, as outlined above, and there is evidence that saliva collected with and without transport media may have comparable accuracy (Bastos 2021).

Clinical pathway

Patients may be tested for SARS-CoV-2 when they present with symptoms, have had known exposure to a confirmed case, or as part of targeted screening of individuals with no known exposure to SARS-CoV-2 for the purpose of attendance at educational establishments or social gatherings. RT-PCR is the primary method for detecting infection during the acute phase of the illness. The standard approach to diagnosis of SARS-CoV-2 infection for individuals presenting with symptoms typical of SARS-CoV-2 or who have had known exposure to a confirmed case is through laboratory-based testing with RT-PCR of swab samples taken from the URT (typically nasopharyngeal, oropharyngeal or combined nasopharyngeal/oropharyngeal). To expand testing capacity where molecular testing is unavailable or associated with long turnaround times, antigen tests on one or a combination of nasal, oropharyngeal or nasopharyngeal samples can be used to identify those who are likely to be infectious with results available in minutes. However, because of the performance characteristics of antigen tests, laboratory-based testing with RT-PCR may be considered necessary to confirm a positive or a negative antigen test result depending on the clinical history and epidemiological setting.

Prior test(s)

Signs and symptoms are used in the initial diagnosis of suspected SARS-CoV-2 infection and to help identify those requiring tests. A number of key symptoms have been suggested as indicators of mild-to-moderate COVID-19, including cough, fever greater than 37.8 °C, headache, breathlessness, muscle pain, fatigue, and loss of sense of smell and taste (Struyf 2022). However, the recently published review of signs and symptoms found good-quality evidence of the accuracy of these symptoms alone or in combination to be lacking (Struyf 2022). Typical symptom profiles may also change with the emergence of new variants (Alford 2021) and as a result of vaccination (Crozier 2021).

Where people are asymptomatic but are undergoing testing for a specific purpose (e.g. universal testing of students as part of a risk-reduction effort) or on the basis of epidemiological risk factors, such as exposure to someone with confirmed SARS-CoV-2 or following travel to more highly endemic countries, no prior tests will have been conducted.

The presence of symptoms has been associated with a higher sensitivity of Ag-RDTs (Dinnes 2022), probably as a result of the presence of symptoms being associated with a higher viral load.

Role of index test(s)

The type of sample collected should be dictated by the manufacturer's instructions for the test technology being used. Often, there is a choice of sample types for use with an individual test technology that is claimed to result in equivalent accuracy by manufacturers. However, the actual performance of different sample types may vary in practice, influenced by sample collection difficulty and the level of training received by sample collectors, as outlined above (Index test(s)). Under these circumstances, it is

important to quantify and understand any variation in accuracy, to inform decisions about which sample type offers the potential for best test performance. Ultimately, when considering the clinical utility of different sampling sites and processes for use on a large scale, accuracy must be balanced against human and material resource needs (training required, time taken for procedure, need for PPE and specialised sampling equipment), supply chain issues (availability of swabs and transport media) and the acceptability of the sampling procedure to patients.

Alternative test(s)

The review was restricted to anatomical sample types and different methods for collecting those that were appropriate for use in ambulatory populations at the time of writing. Lower respiratory tract samples (sputum and bronchiolar lavage) and other nonrespiratory sample types (urine and faecal samples, serum, semen and tears) have not been included, as these sample types have not been considered for routine clinical use in ambulatory populations. The review was also restricted to testing technologies currently in use in ambulatory populations.

This review is one of a series of reviews that cover the range of tests and clinical characteristics being considered in the management of COVID-19 (Dinnes 2022; Ebrahimzadeh 2022; Fox 2022; Struyf 2022). The findings of this review are relevant to reviews concerned with laboratory-based molecular and antigen tests and rapid antigen tests.

Rationale

Estimates of accuracy from this review will help when making choices about specimen types and collection processes to support effective screening and diagnostic interventions for SARS-CoV-2 infection and disease.

OBJECTIVES

To compare the effect of sample site and collection procedure on the sensitivity of molecular or antigen tests in ambulatory populations for the detection of current SARS-CoV-2.

Secondary objectives

Where data were available, we aimed to investigate potential sources of heterogeneity according to population characteristics (healthcare setting, age, symptom status); index test (index sample) characteristics (time of test use post-symptom onset or post-contact with a confirmed case; experience and training of personnel collecting samples; sample collection method) and study design characteristics (use of the same COVID-19 test kit or in house laboratory procedure for both samples in a pair).

METHODS

Criteria for considering studies for this review

Types of studies

We included studies that compared two or more anatomical sampling sites, or two or more sample collection methods from the same anatomical site, from the same participant (within person) using the same type of test technology and from which a 2 x 2 contingency table comparing positive results from each sampling method could be constructed, including:

- single-group studies recruiting participants before disease status has been ascertained; and
- studies based on either patients or samples.

The method for deriving the sensitivity difference from a 2 x 2 contingency table is provided in [Appendix 1](#) and described below under 'Target condition being diagnosed'.

We excluded studies from which 2 x 2 tables could not be derived and studies where recruited individuals were preselected on the basis of testing positive on one of the sample sites being compared (second sampling in known cases). We excluded studies with fewer than 10 samples or participants on the basis that small studies are likely to give unreliable estimates of accuracy. We excluded case-control studies that recruited known cases of COVID-19 and, separately, participants known not to have COVID-19.

We included studies reported in published journal papers and as preprints.

Participants

We included studies recruiting symptomatic people presenting with a suspicion of current SARS-CoV-2 infection and asymptomatic people being tested for infection (close contacts of known SARS-CoV-2 infection, community-based testing programmes including contact tracing and asymptomatic screening). We excluded studies undertaking repeated testing for the purposes of documenting viral shedding.

Index tests

We included upper respiratory tract (URT) samples, saliva samples, oral samples and gargle samples. We included samples acquired and tested by study participants, trained or untrained study personnel, or professionals such as healthcare workers or laboratory scientists, using any collection method, with or without inactivation and stabilisation with transport medium, using any molecular or antigen-based testing method.

We excluded lower respiratory and other non-respiratory samples such as urine, faeces, blood, tears and semen as not suitable for testing in an ambulatory setting.

For the purposes of this review, a sample pair is defined as two samples collected from the same participant tested with the same test technology within the same clinical encounter. Sample pair comparisons encompass:

- two samples, one collected from the nasopharynx or the nasopharynx and combined in the same sample container, and one collected from a different anatomical site; and
- two samples from the same anatomical site collected by personnel with different levels of training or supervision (for example, healthcare worker (HCW) versus self-collection).

Within a sample pair, we defined a reference sample and an index sample collected from the same participant within the same clinical encounter. Where the sample comparison was different anatomical sites, the reference standard was defined as a nasopharyngeal or combined naso/oropharyngeal sample collected into the same sample container and the index sample as the alternative anatomical site. Where the sample comparison was concerned with differences in sample collection method

from the same site, we defined the reference sample as that closest to standard practice for that sample type (for example, nasopharyngeal swab rather than nasopharyngeal aspirate). Where the sample pair comparison was concerned with differences in personnel collecting the sample, the more skilled or experienced operator was considered the reference sample.

Target conditions

The target condition was current SARS-CoV-2 infection (either symptomatic or asymptomatic).

Reference standards

In this review, the combined test results of two different samples being compared (index and reference samples) in the same participant with the same molecular or antigen test constituted the reference standard. The absence of a positive test result on two or more different sample types taken in the same clinical encounter in the same participant was assumed to indicate an absence of SARS-CoV-2 infection. The analytical approach to this review precluded estimation of specificity. We assumed that the impact of false negatives and false positives on estimates of the *difference* in sensitivity for different sample types should be minimal, provided the molecular or antigen testing method was the same (test type, gene targets, test positivity threshold, kit manufacturer) for each sample in a pair, taken in the same clinical encounter.

Search methods for identification of studies

Due to the living nature of this Cochrane series of reviews, the sources used for searching changed over time. We used two main sources for our electronic searches. These strategies were devised with the help of an experienced Cochrane Information Specialist with broad diagnostic test accuracy review expertise (RSp). Searches aimed to identify all articles related to COVID-19 and SARS-CoV-2 and were not restricted to those evaluating a particular type of test. The searches, therefore, did not use terms specifically focused on an index test, diagnostic accuracy or study methodology, to provide information to several reviews belonging to this series simultaneously ([Dinnes 2022](#); [Fox 2022](#); [Struyf 2022](#)).

Electronic searches

Cochrane COVID-19 Study Register searches

We used the Cochrane COVID-19 Study Register (covid-19.cochrane.org) for searches conducted from the inception of the register to 28 March 2020. At that time, the register was populated by searches of PubMed, as well as trials registers at US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (apps.who.int/trialsearch). Search strategies were designed for maximum sensitivity to retrieve all human studies on COVID-19 and SARS-CoV-2 with no language limits ([Appendix 2](#)). To ensure comprehensive coverage, we also downloaded records from the 'Bern feed' from 1 January to 28 March 2020 and de-duplicated them against those obtained via the Cochrane COVID-19 Study Register. We decided to continue with the Bern feed given the enormous number of COVID-19 studies available only as pre-prints at the time.

COVID-19 Living Evidence Database from the University of Bern

From 28 March 2020 to 17 February 2022, we used the COVID-19 Open Access Project living evidence database (COAP) from the

Institute of Social and Preventive Medicine (ISPM) at the University of Bern ([COVID-19 Open Access Project \(COAP\) 2020](#)). The database was constructed from daily (Monday to Friday) systematic searches of Embase via OVID, MEDLINE via PubMed, bioRxiv and medRxiv. The strategies as described on the COAP website are reported in [Appendix 3](#).

Due to the increased volume of published and pre-print articles, from 25 May 2020 onwards, we used artificial intelligence text analysis to conduct an initial classification of documents, based on their title and abstract information, for relevant and irrelevant documents ([Appendix 4](#)).

Other electronic sources

Before 28 March 2020 (when we began using the "Bern feed"), we identified Embase records through CDC, Stephen B Thacker CDC Library, COVID-19 Research Articles Downloadable Database (cdc.gov/library/researchguides/2019novelcoronavirus/researcharticles.html). We de-duplicated them against results from the Cochrane COVID-19 Study Register ([Appendix 2](#)). We also checked our search results against two additional repositories of COVID-19 publications up to 30 September 2020:

- Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) "COVID-19: Living map of the evidence" (eppi.ioe.ac.uk/COVID19_MAP/covid_map_v4.html); and
- Norwegian Institute of Public Health "NIPH systematic and living map on COVID-19 evidence" (www.norgesk.no/forskningskart/NIPH_diagnosisMap.html).

Both repositories allow their contents to be filtered according to studies potentially relating to diagnosis.

Searching other resources

We contacted or accessed the websites of independent research groups undertaking test evaluations, including studies co-ordinated by FIND (finddx.org/covid-19/sarscov2-eval) and the Diagnostics Global Health listing of manufacturer-independent evaluations of antigen detecting rapid diagnostic tests (Ag-RDTs) for SARS-CoV-2 (diagnosticsglobalhealth.org).

Data collection and analysis

Selection of studies

A team of experienced systematic review authors from the University of Birmingham screened the titles and abstracts of all records retrieved from the literature searches. Two review authors (CD, IA, MM-H, AC, DB-G) independently screened studies in [Covidence](#). A third, senior review author resolved any disagreements (CD, IA). We tagged all records selected as potentially eligible according to the Cochrane COVID-19 diagnostic test accuracy review(s) for which they might be eligible, and we then exported them to separate [Covidence](#) reviews for each review title. We obtained the full texts for all studies flagged as potentially eligible. Two review authors independently screened the full texts for one of the COVID-19 biomarker reviews (molecular, antigen, antibody tests or sampling). We resolved any disagreements about study inclusion through discussion with a third review author.

Up to September 2020, screening was conducted across all Cochrane COVID-19 DTA biomarker reviews (molecular, antigen,

antibody tests or sampling), using tagging of records according to the review(s) for which they might be eligible. From September 2020 onwards, review-specific searches were implemented such that screening was conducted without the requirement for study tagging for different reviews.

Data extraction and management

One review author extracted the characteristics of each study, which a second review author checked (CD, MM-H, IA, AC, DB-G).

Two review authors independently performed data extraction of 2 x 2 contingency tables of positive and negative results by sample type ([Appendix 1](#)). Disagreements were resolved by discussion. Where possible, we separately extracted data according to setting, age, symptom status, time post-symptom onset or post-contact with a confirmed case, training of the person collecting the index test sample, use of transport medium and whether identical manufacturer testing kits or in-house laboratory testing procedures were used for each sample in a pair.

Where there was uncertainty about the eligibility of a study or where studies were considered eligible, but we were not able to extract 2 x 2 contingency tables, we attempted to contact authors for the required information. A total of five authors were successfully contacted for clarification about inclusion decisions.

Assessment of methodological quality

Two review authors independently assessed the risk of bias and applicability concerns using the QUADAS-2 ([Whiting 2011](#)) and QUADAS-C ([Yang 2021](#)) checklists, tailored to this review ([Appendix 5](#)) (CD, MM-H, IA, AC, DB-G). Disagreements were resolved by discussion.

In assessing the risk of bias in included studies, we considered methods for participant selection into studies (participant selection domain), methods for comparing each index and reference sample pair in a study (index test domain) and the flow of participants through a study (flow and timing domain).

For this review, the combined positive results of index and reference samples were used as a proxy for the number of cases of SARS-CoV-2 in a study population to allow estimation of the sensitivity of each sample type in a pair. As part of tailoring of QUADAS-2 for this review, we therefore did not use the reference standard domain and instead added questions to the index test domain to assess the risk of bias for the index and reference sample pair comparison. In assessing the applicability of study findings, we considered whether study participants were representative of individuals at the point of testing to make a diagnosis of SARS-CoV-2 (in any setting), that testing was done with available technology, and the sampling process was described in sufficient detail to be replicable.

For participant selection, we considered that, ideally, studies examining the accuracy of different sampling techniques for the diagnosis of SARS-CoV-2 should prospectively recruit a representative (random or consecutive) sample of participants who would undergo testing for the diagnosis of SARS-CoV-2 in practice (intended use setting). We excluded diagnostic case-control studies recruiting people with and without the target condition, as these studies are known to overestimate test accuracy ([Rutjes 2006](#)). Individuals should not be excluded from a study population because they are difficult to diagnose or because

they have difficulty complying with a sample technique. Similarly, study populations should not be enriched with individuals who are less likely (convenience sample with other disease) or more likely (having recently received a previous positive SARS-CoV-2 test result) to have the target condition.

To be certain that any observed differences in accuracy between a sample pair were due to the sampling site or procedure, all other elements of the testing process should be comparable. The order in which certain sample types are collected may be important to avoid contamination (for example, for a comparison between nasal and nasopharyngeal sites or between oropharyngeal and nasopharyngeal sites). Similarly, although recent research indicates that repeated sampling of the same sample site does not reduce SARS-CoV-2 test performance ([Levy 2021](#)), care should be taken if there are implications from learning effects for comparisons of different collection procedures from the same sample site. These effects can be mitigated using random ordering of sample collection or sampling from opposite nares for nasopharyngeal and nasal sample types. Factors aside from the sample site and sampling procedure that could impact on accuracy (specimen storage and transport including use of transport medium, extraction and testing kits, gene targets and test positivity threshold) should be detailed. Test results (presence or absence of SARS-CoV-2) from comparison sample sites or sample collection methods should be interpreted blind to each other.

Studies should report data for all study participants, including those where the sample taken was inadequate, the SARS-CoV-2 test was invalid, or the test result was indeterminate, to allow assessment of differences in the proportions and reasons for missing data between sample sites or sample procedures being compared. Studies should report whether results relate to participants (one sample per participant), or samples (multiple samples per participant).

For assessment of applicability, the study setting is an indicator of the spectrum and prevalence of disease. Setting is also a proxy for other elements of the sampling and testing process that may have an impact on test accuracy, such as operator experience and skill and practical challenges associated with taking and processing samples. Studies should detail the setting in which testing is taking place (for example, community, primary care, dedicated

COVID-19 testing facility, hospital outpatient or inpatient). The symptom status of participants should be documented, as well as time since symptom onset and, if relevant, exposure history (time post-contact with a confirmed case of SARS-CoV-2). Studies on asymptomatic people at risk of infection should document the time of exposure or, where tests are being applied for screening purposes, the indication for screening should be provided (for example, targeted screening in educational settings).

Statistical analysis and data synthesis

We assumed that the false positive rate from molecular and antigen tests would be low for all sample collection methods. Further, we assumed that for each sample pair, tested under the same laboratory conditions (extraction, molecular or antigen testing kit or in-house laboratory procedure, gene targets and thresholds), that any differences in sensitivity between sample types, not driven by the sampling process itself, would be negligible.

The combined results of a SARS-CoV-2 test (molecular or antigen tests) on two or more different sample sites constituted the reference standard. We estimated the sensitivity of each index sample site (nasopharyngeal/oropharyngeal collection combined in the same sample container, nasopharyngeal alone, oropharyngeal alone, oropharyngeal/nasal samples combined in the same sample container, nasal, saliva, oral, gargle) or the person collecting the sample (self-collection, supervised self-collection, healthcare professional (HCW)) in a pair, as the number of test positives from that sample site/sample collection operator divided by the total number of test positives (positive on either sample in a pair). Where indeterminate results were reported, these were classed as positive for the purposes of the primary analyses, reflecting the fact that indeterminate results are more aligned to a positive rather than a negative test result in terms of clinical actions.

The table below shows the cross-classification of the results for a comparison of two anatomical sampling sites comprising a reference sample type (for example, nasopharyngeal or nasopharyngeal/oropharyngeal combined in the same sample collection container) and the alternative sample type (such as saliva, nasal swabs, etc.) for the outcome of being positive or negative for current SARS-CoV-2 infection.

		Reference sample type		Total
		Positive	Negative	
Alternative sample type	Positive	a	b	a + b
	Negative	c	d	c + d
	Total	a + c	b + d	a + b + c + d

Using the notation in the table above, the sensitivity difference (SD) was calculated as:

$$SD = (b - c)/n$$

where n is the total number who tested positive on either of the sample types and not the number of cases ([Appendix 1](#)).

We present estimates of the difference in the sensitivity (reference sample (%) minus index sample sensitivity (%)) in a pair and as an average across studies for each index sampling method using

forest plots and tables. If the reported difference in sensitivity is negative, the index sample misses more cases of SARS-CoV-2 infection compared to a nasopharyngeal sample. If the difference in sensitivity is positive, more cases of SARS-CoV-2 infection (true positives (TP)) are detected by the index sample compared to the nasopharyngeal sample. We expressed the difference in sensitivity % in percentage points such that, for example, a reference sample sensitivity of 98% compared to an index sample sensitivity of 96% would be presented as "-2 percentage points." As heterogeneity is apparent in many analyses, these summary estimates must be interpreted as the average of a distribution of values.

We did not make any formal comparisons between the sensitivity of index sampling sites (nasopharyngeal, oropharyngeal, oropharyngeal/nasal, nasal, saliva, oral, gargle) or sample collection operator (self-collection, supervised self-collection, healthcare professional) because of heterogeneity in study participants, index sample type, collection procedures and reference sample types used.

We obtained the pooled sensitivity difference and its 95% confidence intervals using the inverse variance random-effects approach (DerSimonian 1986). Statistical heterogeneity was measured using the between-study variance, τ^2 (τ^2) from the random-effects analyses (Rucker 2008). In contrast to I^2 (the percentage of variability due to heterogeneity between studies rather than sampling error), τ^2 is a measure of the underlying between-study variance. Unlike I^2 , therefore, τ^2 is not dependent on the size of the included studies, and does not tend to 1, as sampling error tends to 0 when included studies are large. The square root of τ^2 , τ , is measured in the same units as a study outcome and thus τ^2 can be directly used to quantify variability. In a review, we can therefore comment on the relative heterogeneity of one meta-analysis compared to another measuring the same outcome.

When the within-study variance of the sensitivity difference equals zero, it leads to the exclusion of the study from the calculation of the pooled estimates, potentially introducing bias. Therefore, a correction is applied to this zero variance, allowing those studies to be included in the pooled estimates. Further details on the data synthesis techniques are given in [Appendix 1](#).

All statistical analyses were performed using Stata/SE 17.0 (STATA).

Investigations of heterogeneity

We examined heterogeneity between studies by visually inspecting the forest plots for the difference in sensitivity. Where adequate data were available within anatomical sample sites (more than three studies per subgroup), we used univariable random-effects meta-regression to statistically compare sensitivity differences between subgroups according to the following characteristics.

- Participants
 - Age: adult (≥ 18 years if reported); child (< 18 years if reported); mixed; unclear
 - Symptom status: symptomatic; asymptomatic; mixed; unclear
- Index test
 - Time post-symptom onset
 - for symptomatic participants: ≤ 1 week; ≤ 2 weeks; ≤ 3 weeks; not stated

- for asymptomatic participants time post-contact with a confirmed case, if applicable: ≤ 1 week; ≤ 2 weeks; ≤ 3 weeks; not stated
- Operator: self-collection (unsupervised); supervised (by a person trained in sample collection) self-collection; healthcare worker (HCW); not stated
- Addition of medium to sample: transport medium; saline; water; none (direct); not stated
- Variation in sample collection
 - for nasal samples: anterior; mid-turbinate; not otherwise specified
 - for saliva samples: spit; drool; salivate; deep throat; not otherwise specified
 - for oral samples: buccal; tongue; not otherwise specified

Sensitivity analyses

When within-study variance of the sensitivity difference equals zero, it leads to the exclusion of the study from the calculation of the summary estimates, potentially introducing bias. We performed a sensitivity analysis whereby we calculated pooled estimates without the zero variance correction, therefore excluding studies with a within-study variance of the sensitivity difference of zero. We then compared results between the main analysis with the correction applied and the sensitivity analysis without the correction.

We also undertook sensitivity analysis to investigate the effect of using different manufacturer kits or in-house laboratory procedures on the same SARS-CoV-2 test technology for different samples in a pair. Results were compared with the main analysis (evaluations irrespective of whether the same test kit had been used or in-house laboratory procedures followed) and the sensitivity analysis (eliminating studies where different kits or different in-house laboratory procedures had been used).

Assessment of reporting bias

We made no formal assessment of reporting bias.

Summary of findings

We summarised key findings in a [Summary of findings 1](#), indicating the strength of evidence for each index sample type, findings, and highlighted important gaps in the evidence.

RESULTS

Results of the search

We screened a total of 37,191 unique records (published or preprints). Of 1871 records selected for further assessment for inclusion in any of the four molecular, antigen or antibody test reviews, we identified 318 full-text reports requiring assessment for inclusion in this review. See [Figure 1](#) for the PRISMA flow diagram of search and eligibility results. We contacted the authors of five studies (seven evaluations) for information to clarify eligibility concerning participant selection or study design. Four studies (six evaluations) were subsequently included: [Desai 2021\(a\)\[A\]](#); [Desai 2021\(a\)\[B\]](#); [Desai 2021\(a\)\[C\]](#); [Desai 2021\(b\)](#); [Smith-Jeffcoat 2021](#); [Teo 2021 \(a\)](#); [Teo 2021 \(b\)](#); [Walker 2021](#) and one study (one evaluation) was excluded because the study population was pre-selected ([Zobrist 2022](#)).

Figure 1. PRISMA flow diagram

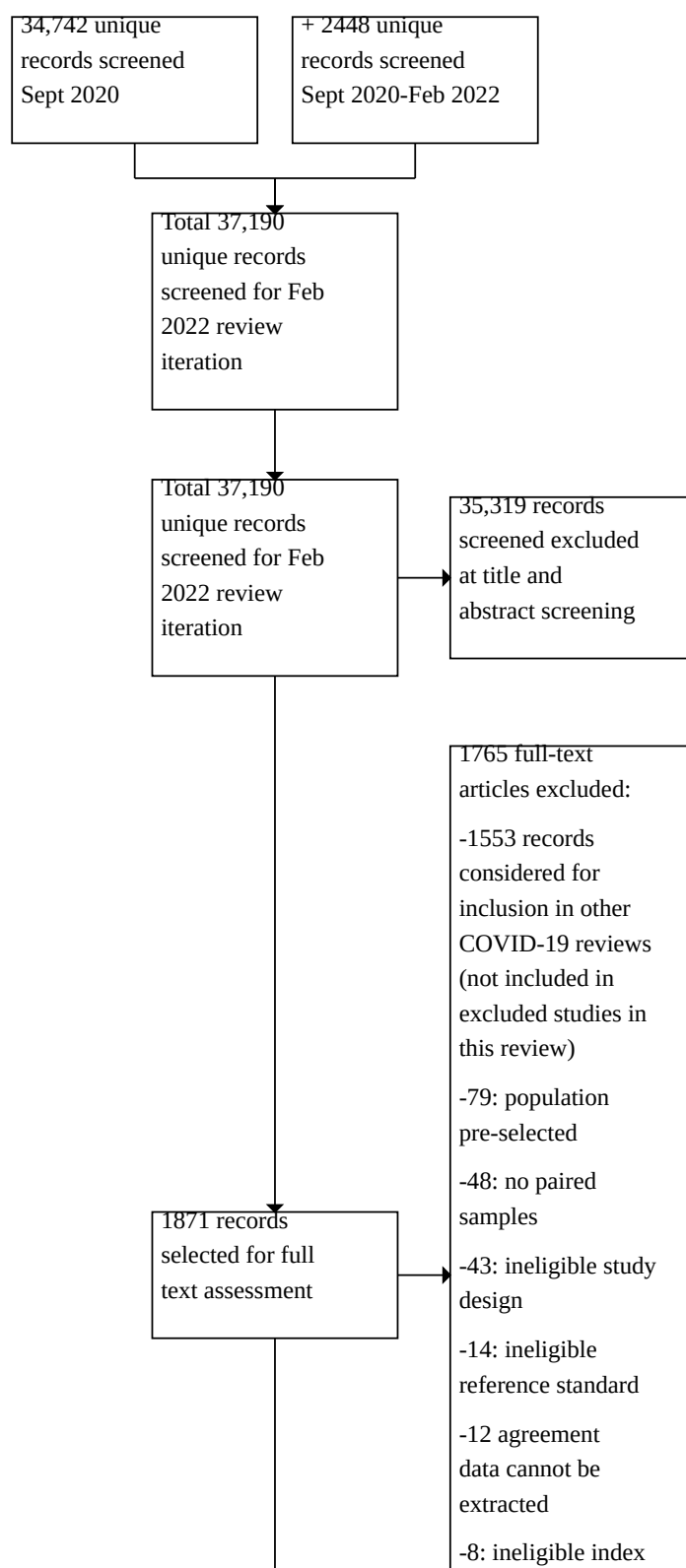
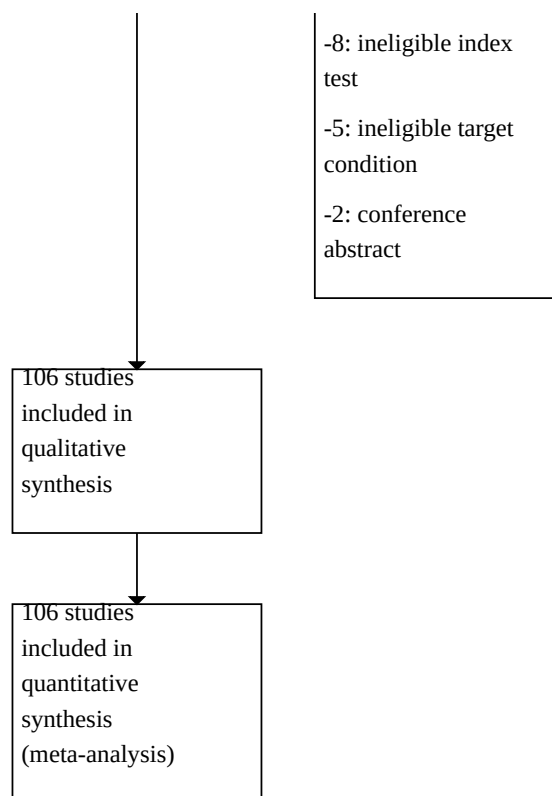


Figure 1. (Continued)



We included 106 reports in this review, and we excluded 212 that did not meet our inclusion criteria. Exclusions were mainly because study populations were pre-selected, i.e. samples were obtained from previously confirmed cases rather than for the primary diagnosis of SARS-CoV-2 ($n = 79$), because paired samples were not used ($n = 49$), or because of an ineligible study design (healthy controls or multiple samples per patient ($n = 43$)). The reasons for exclusion of all 211 publications are provided in [Excluded studies](#).

Of the 106 study reports, seven were only available as preprints at the time of writing ([AbdulRahman 2020a](#); [Becker 2020](#); [Bikos 2021](#); [Da Silva 2022](#); [Fernández-Pittol 2020](#); [Marx 2021 \(a\)](#); [Miller 2020](#)). Four study reports were independent evaluations of SARS-CoV-2 antigen detection rapid diagnostic (Ag-RDT) tests made available to us by FIND, the global alliance for diagnostics (www.finddx.org): [FIND \(a\) 2021](#); [FIND \(b\) 2021](#); [FIND \(c\) 2021\(a\)](#); [FIND\(c\) 2021 \(b\)](#); [FIND\(s\) 2021](#)). For the purposes of this review, each participant contributes a sample pair (one index sample and one reference sample) and 'index tests' are the different anatomical sample sites or collection processes. The 106 included study reports related to 135 participant cohorts (a study reporting results for participants in multiple settings) and 154 separate evaluations of index tests (17 of the 135 participant cohorts evaluated two index tests and two of the 135 participant cohorts evaluated three index tests).

When naming studies, we use the letters (a), (b) and (c) to indicate data from different participant cohorts in the same study report. We use the letters [A], [B] and [C], etc., in square brackets to

indicate data on multiple index tests evaluated amongst the same participants.

Description of included studies

This review includes 106 studies reporting 154 evaluations and 60,523 sample pair comparisons, of which 11,045 had SARS-CoV-2 infection. Of 154 included evaluations, more than half were concerned with the accuracy of saliva samples (90/154, 58%), followed by nasal samples (37/154, 24%), oropharyngeal (7/154), gargle (6/154), oral (6/154), mixed nasal/oropharyngeal (4/154), and 4/154 evaluations were concerned with the effect of operator training on accuracy ([Table 1](#); [Table 2](#); [Table 3](#); [Table 4](#)).

Most of the studies were conducted in Europe (35/106, 33%) and the USA (29/106, 27%). Nineteen (18%) studies were conducted in Asia, 15 (14%) in South America, four in Canada, two in Africa and two in Australia ([Appendix 6](#)).

Study design

See [Appendix 6](#).

Most evaluations were of a single-group design, recruiting participants suspected of having SARS-CoV-2 infection. Four evaluations employed a two-group design, where participants tested for suspected SARS-CoV-2 infection were subsequently recruited after a positive or negative reference (nasopharyngeal) sample test result and received the index sample collection within a 24-hour period ([Guclu 2020 \(a\)](#); [Kojima 2020](#); [McCormick-Baw](#)

2020; McCulloch 2020). Two evaluations enriched a single group of participants suspected of SARS-CoV-2, either with participants positive on a reference (nasopharyngeal) sample within the preceding 24 hours (Callahan 2021(a)), or with samples from participants on dedicated COVID-19 inpatient wards whose disease status (suspected or confirmed positive) at the time of sampling was unclear (McCormick-Baw 2020).

Most evaluations were prospective (124/154, 81%), nine (6%) were retrospective, one study employed a mixed prospective and retrospective design and in 20 (13%) evaluations this was unclear. Almost all (150/154, 97%) evaluations evaluated the effect on accuracy of different anatomical sampling sites. Of these, 130/150 (87%) used a nasopharyngeal swab and 20/150 (13%) used a combined naso/oropharyngeal swab as a reference sample site. Four evaluations assessed the difference in accuracy between operators with different levels of expertise sampling the same site. Two of these four evaluations were concerned with the effect of operator experience on the accuracy of nasopharyngeal samples (Abdollahi 2020a; Amoo 2021), one on oropharyngeal samples (Abdollahi 2020b), and one on saliva samples (Kojima 2020).

Setting for testing

Some evaluations were conducted in dedicated COVID-19 testing clinics or drive-through venues (43/154, 28%), or in ambulatory hospital settings (38/154, 25%). Twenty-one (14%) evaluations were recruited from community settings (primary care, participant homes or not otherwise specified), 20 (13%) included participants from mixed settings and, in 17 (11%), the study setting was unclear. A minority of evaluations was conducted in inpatient settings (9/154, 6%) as part of targeted screening (5/154, 3%) or contact tracing (1/154, < 1%). The preponderance of evaluations in dedicated COVID-19 testing sites and ambulatory settings was seen across all sample types/index tests.

Missing data and indeterminate results

Forty-eight of 154 (31%) evaluations reported invalid or uninterpretable samples. Evaluations of saliva (36/90, 40%), and gargle (2/6, 33%) samples and evaluations of the effect of operator training on accuracy (1/3, 33%) contributed slightly more invalid or uninterpretable results compared to nasal samples (9/37, 24%). For saliva, invalid samples were most often a result of inadequate volume or hyper viscosity of samples. For other sample types, the reason for invalid or uninterpretable results was not provided. Twenty-one of 154 (14%) evaluations (13 saliva, six nasal, one oral and one evaluation evaluating the effect of operator training on accuracy) reported lost samples.

Eighteen of 154 (12%) evaluations (16 saliva and two nasal) reported the occurrence of indeterminate test results. For the purposes of analysis in this review, indeterminate results were classed as positive (see [Statistical analysis and data synthesis](#)).

Participant characteristics

See [Appendix 6](#).

Participant demographics

More than half of evaluations (91/154, 59%) were conducted on adults, 28/154 (18%) were conducted in mixed populations, and seven of 154 (4%) (six self-collected saliva and one healthcare professional-collected nasal) were conducted on children. In 28 (18%) evaluations, the age of participants was unclear.

Symptoms and exposure history

Just under half of the evaluation cohorts (71/154, 46%) were conducted on mixed symptomatic and asymptomatic participants, one-third (51, 33%) on symptomatic participants, seven (5%) on asymptomatic participants and, in 25 (16%) of evaluation cohorts, symptom status was not reported. Forty of 154 evaluation cohorts (26%) reported whether participants had been exposed to a confirmed case of SARS-CoV-2. Of the 37/40 evaluations reporting the proportion of participants exposed, the median was 22%, ranging between 0% (Teo 2021 (a)) and 100% (Boutros 2021 (b); Marquette 2021 (a); Marquette 2021 (b); Marquette 2021 (c); Teo 2021 (b)) in contact tracing settings.

Timing of testing in relation to symptom onset or contact with health services

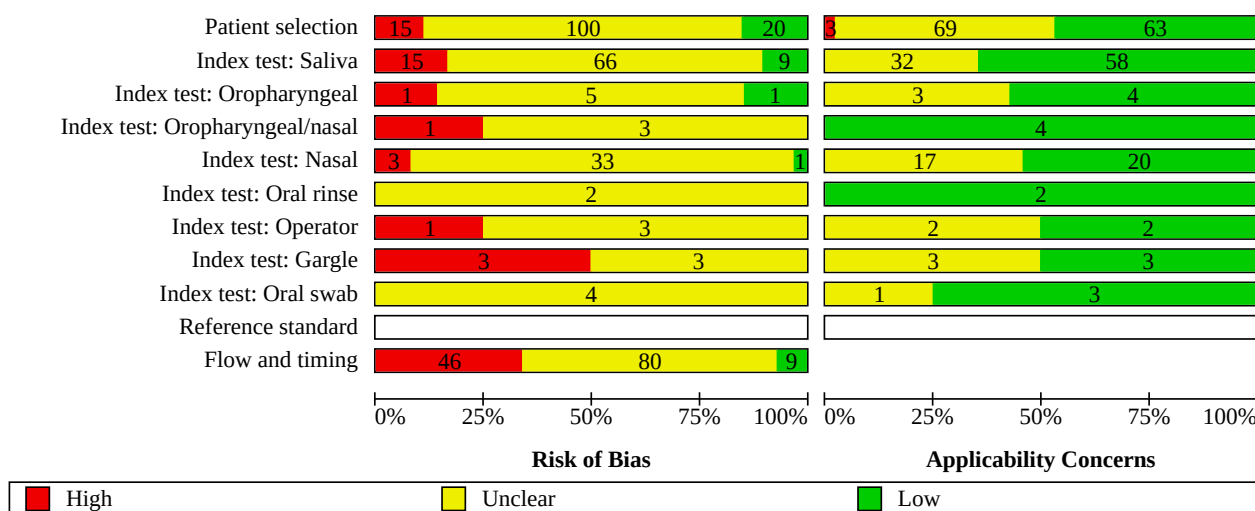
In more than half of evaluations (96/154, 62%), the time of sampling in relation to symptom onset was not stated. Of the 58 evaluations with 'time of sampling post-symptom onset' reported, 39/58 (67%) were within one week of onset, 13/58 (22%) were within two weeks and 6/58 (10%) were within three weeks. The preponderance of evaluations within one week post-symptom onset was observed across all sample types/index tests.

Index tests

Index sample collection method

See [Appendix 6](#).

The level of detail provided about sample collection varied considerably across evaluations. In 62% (96/154) of evaluations, we considered sufficient detail was provided to allow replication of sample collection or a commercial kit was used ([Figure 2](#)). This varied from 100% for oropharyngeal/nasal (4/4) and oral rinse (2/2) samples, to 75% (3/4) for oral samples, 64% (58/90) for saliva samples, 57% (4/7) for evaluations evaluating the effect of operator experience, 54% (20/37) for nasal samples, and 50% for operator (2/4) and gargle (3/6) index samples. Examples of information provided by evaluations included the angle and depth to which swabs should be inserted, whether one or both nares/sides of the oropharynx should be swabbed, the number of times swabs should be rotated, whether there should be a delay between eating and drinking and saliva collection, whether collection of saliva samples should be preceded by coughing, and the volume of saliva sample required.

Figure 2. Methodological quality graph: all sample types

Most of the index samples in evaluations were either self-collected (88/154, 57%) or self-collected whilst supervised by a healthcare worker (HCW) (36/154, 23%). Only 18 (12%) evaluations reported sample collection by a HCW: 11/37 (30%) for nasal samples, four of seven (57%) for oropharyngeal samples, two of four (50%) mixed nasal/oropharyngeal samples, and in one of 90 (1%) saliva evaluations. In 13/154 (8%) evaluation cohorts, the person collecting the sample was not stated.

In 69 of the 90 evaluations of saliva compared to nasopharyngeal or naso/oropharyngeal samples combined in the same collection container, five different collection methods were described. Where described, many (34/69, 49%) collection methods involved spitting into a collection device. Drooling, salivating and deep throat were described by 11 (16%) each, whilst combined swab and drool collection was described by one evaluation. Twenty of the 90 evaluations of saliva (22%) reported using a commercially available collection device, including Salivette tubes (SARSTEDT Ag & Co, Numbrecht, Germany) (n = 6; [Aita 2020](#); [Fernández-Pittol 2020](#); [Huber 2021 \(a\)](#); [MeloCosta 2021 \(a\)](#); [MeloCosta 2021 \(b\)](#); [MeloCosta 2021 \(c\)](#); [Vlek 2020](#); [Walker 2021](#)); Saliva and RNA Collection and Preservation device (Norgen Biotek, Thorold, Ontario, Canada) (n = 5; [Mestdagh 2021 \(a\)\[A\]](#); [Mestdagh 2021 \(a\)\[B\]](#); [Mestdagh 2021 \(c\)\[A\]](#); [Mestdagh 2021 \(c\)\[B\]](#); [Mestdagh 2021 \(d\)\[A\]](#); [Mestdagh 2021 \(d\)\[B\]](#); [Mestdagh 2021 \(e\)\[A\]](#); [Mestdagh 2021 \(e\)\[B\]](#); [Mestdagh 2021 \(f\)\[A\]](#); [Mestdagh 2021 \(f\)\[B\]](#)); OMNIgene-ORAL, OM-505 (DNA Genotek, UK) (n = 2; [Becker 2020](#); [Miller 2020](#)); the Orasure Oragene DX (OGD-510 device, Canada) (n = 2; [Boerger 2021](#); [Hamilton 2021](#)), and the Saliva collection Kit (Comedical, Trento, Italy) (n = 2; [Fronza 2021 \(a\)](#); [Fronza 2021 \(b\)](#)). One evaluation each used the Spectrum DNATM saliva collection device (Spectrum Solutios, Draper, UT) ([Bruxvoort 2021](#)), the OraCollect RNA, DNA Genotek, (Kanata, Ontario, Canada) ([Mestdagh 2021 \(b\)\[A\]](#); [Mestdagh 2021 \(b\)\[B\]](#)), the DNA/RNA Shield Saliva Sputum Collection Kit eDX (Zymo Research, Irvine, CA) ([Sahajpal 2021](#)), and the SDNA 1000 Saliva Collection Device (Solutions LLC, USA) ([Torres 2021](#)).

In 34 of the 37 (92%) evaluations of nasal samples, the precise location of collection was reported: 19/37 (51%) evaluations

sampled from the mid-turbinate and 15/37 (41%) sampled from the anterior nares.

Reference sample site

See [Table 2](#), [Table 3](#) and [Table 4](#).

For the 151 evaluations comparing the accuracy of different anatomical sites, most (131/151, 87%) used HCW-collected nasopharyngeal samples as the reference sample site, with the remainder (20/151, 13%) using a combined oropharyngeal / nasopharyngeal swab in the same collection container. In three of 154 evaluations, the effect of sample operator on the accuracy of samples from the same anatomical sample site was examined: HCW compared to self-collection of oropharyngeal samples ([Abdollahi 2020a](#); [Abdollahi 2020b](#)), HCW compared to self-collection of nasopharyngeal samples ([Amoo 2021](#)), and supervised self-collection compared to unsupervised self-collection of saliva ([Kojima 2020](#)).

Index sample storage and transport

See [Table 2](#), [Table 3](#) and [Table 4](#).

Approximately half of samples were collected and stored in transport media (79/154, 51%). Sampling without the use of viral transport media was reported explicitly in 57/154 (37%) collections. In 50 of 57 evaluations not using transport media, the sample was collected and stored dry (43 saliva, seven nasal), and in seven the sample was collected into either water or saline (three gargle, two saliva, two oral rinse). Eighteen of 154 evaluations did not report whether viral transport media were used.

Testing methods used for sample comparisons

See [Table 2](#), [Table 3](#) and [Table 4](#).

A majority (140/154; 91%) of evaluations used RT-PCR to detect SARS-CoV-2 in study samples. Four evaluations used isothermal techniques with saliva and nasal samples ([Desai 2021\(a\)\[A\]](#); [Desai 2021\(a\)\[B\]](#); [Desai 2021\(a\)\[C\]](#); [Desai 2021\(b\)](#)), two evaluation cohorts used Transcription-Mediated Amplification (TMA) with saliva samples ([Banerjee 2021](#); [Migueres 2021 \(a\)](#)), and eight

evaluations used Ag-RDT tests with nasal samples (FIND (a) 2021; FIND (b) 2021; FIND (c) 2021(a); FIND(c) 2021 (b); FIND(s) 2021, Klein 2021; Labhardt 2022; Lindner 2021).

In 13 of 154 (8%) evaluations (seven saliva, three nasal, two oral and one oropharyngeal), the validity of the comparison was potentially undermined because the method of RNA extraction and/or the RT-PCR testing kit differed between index and reference sample sites (Becker 2020; Bikos 2021; De Oliveira 2021; Herrera 2021; McLennan

2022; Pere 2020; Rajh 2021[A]; Rajh 2021[B]; Rajh 2021[C]; Sahni 2021; Wehrhahn 2020 (2 evaluations); Williams 2020).

Where reported, the test positivity threshold used was the same for both samples in a comparison. The test positivity threshold ranged from $Ct \leq 27.5$ (Kannian 2021) to $Ct \leq 50$ (Desai 2021(a)[A]; Desai 2021(a)[B]; Desai 2021(a)[C]; Desmet 2020).

Methodological quality of included studies

See Figure 2, Figure 3, Figure 4, Figure 5 and Appendix 7.

Figure 3. Methodological quality graph: saliva

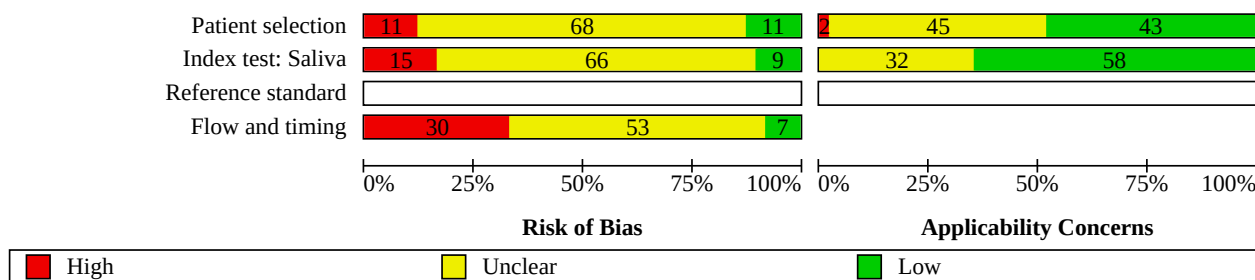


Figure 4. Methodological quality graph: nasal

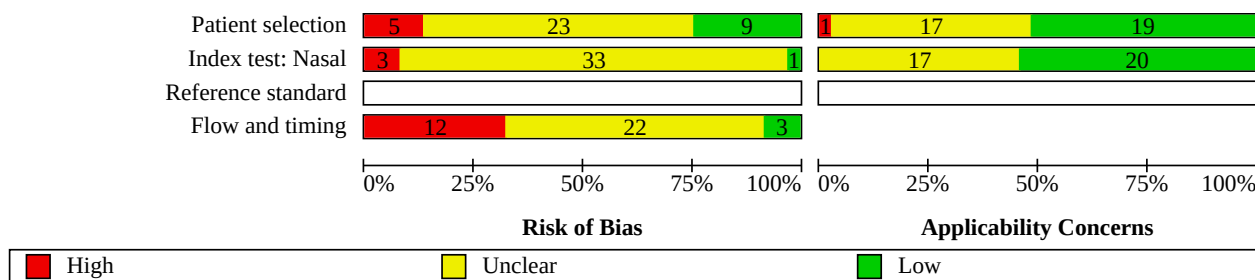
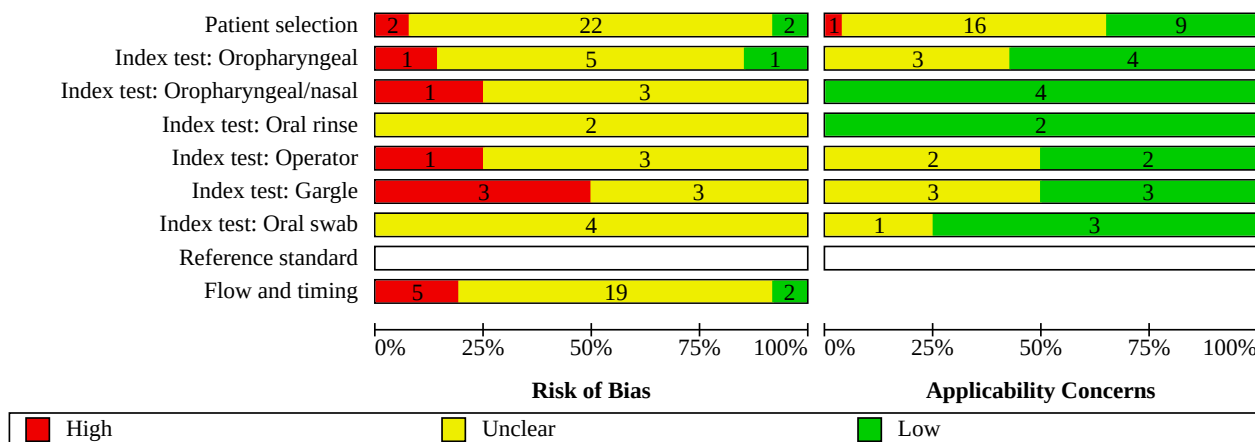


Figure 5. Methodological quality graph: oropharyngeal, nasal/oropharyngeal, oral rinse, operator, gargle, oral swab



We reported quality assessment for the participant and flow and timing domains at the participant cohort level ($N = 135$) and quality assessment for the index (sample) test domain at the evaluation level ($N = 154$); [Figure 2](#); [Figure 3](#); [Figure 4](#); [Figure 5](#). See [figure 6](#), [figure 7](#) and [figure 8](#) in [Appendix 7](#) for separate summary plots by sample type. The basis for responses to individual signalling questions is detailed in the [Characteristics of included studies](#) (see [Appendix 6](#)).

We judged only 4/154 (3%) evaluations as having low risk of bias overall ([Boutros 2021\(a\)](#); [Boutros 2021 \(b\)](#); [Lindner 2021](#); [Marquette 2021 \(a\)](#)). Fifty of 154 (32%) evaluations (32 saliva, 11 nasal, two oropharyngeal, two oropharyngeal nasal and one each of gargle, oral rinse and operator) were judged to be of low applicability concern.

Participant selection

In three-quarters of participant cohorts (100/135; 74%), the risk of bias was considered unclear because of poor reporting of recruitment and inclusion criteria. The risk of bias was judged as high in 15/135 (11%) of participant cohorts because of one or more of the following features: non-consecutive or non-random sampling ($n = 9$); enriching participant cohorts with reference sample positive samples prior to testing stored index samples (creating a two-group design) ($n = 4$); or because of inappropriate exclusions, for example, participants who were not able to provide a sufficient volume of saliva ($n = 5$).

We had low concerns about the applicability of participants in approximately half (63/135, 47%) of cohorts and the applicability of participants to the review question was unclear in half (68/135, 50%) of cohorts. In three of 135 cohorts, participants were considered to be of high applicability concern because of enrichment of the sample with an unknown number of reference sample (nasopharyngeal) positives ([Callahan 2021\(e\)](#); [Wehrhahn 2020](#)) or selective sampling from a primary care referred suspected sample ([Miller 2020](#)).

Index test

In many (119/154; 77%) evaluations, the risk of bias in the index test domain was considered unclear. Twenty-four of 154 (16%) evaluations were considered to be at high risk of bias in the index test domain because of one or more of the following features: lack of blinding between index and reference samples ($n = 3$), the use of different SARS-CoV-2 testing kits ($n = 6$), or because the ordering of collection of samples was likely to influence the accuracy of the index sample test result; for example, nasal samples being collected after nasopharyngeal samples in the same nostril ($n = 11$).

For many evaluations, concerns about the applicability of the index test domain were low (94/154, 61%). Fifty-eight of 154 (38%) evaluations were considered to be at unclear applicability concern, whilst no evaluations were considered to have high applicability concern.

Flow and timing

Poor reporting precluded judgements about risk of bias for participant flow and timing in many (80/135, 59%) participant

cohorts. In particular, there was a lack of detail about participant flow; for example, using a Standards for Reporting Diagnostic Accuracy Studies (STARD)-style participant flow diagram. Forty-six of 135 (34%) participant cohorts were at high risk of bias because of one or more of the following features: the proportion and reasons for missing test results being different across index and reference samples being compared ($n = 31$), not all tested participants being included in the analysis ($n = 12$), or participants not receiving all index samples where participants received index tests at multiple time points ($n = 12$). Only nine of 135 participant cohorts were considered to be at low risk of bias in the participant flow and timing domain.

Findings

Key findings can be found in the [Summary of findings 1](#). Overall, a total of 60,523 sample pairs contributed to 154 evaluations. A total of 40,342 sample pairs contributed to the 90 saliva evaluations; 12,979 sample pairs contributed to the 37 nasal evaluations; 2522 sample pairs contributed to the seven oropharyngeal evaluations; 2138 sample pairs contributed to the six gargle evaluations; 701 sample pairs contributed to the four combined nasal/oropharyngeal evaluations; 360 sample pairs contributed to the four evaluations assessing the effect of operator experience on the accuracy of nasopharyngeal, oropharyngeal or saliva sample collection; 238 sample pairs contributed to the two oral rinse evaluations; and 1242 sample pairs contributed to the four oral swab evaluations. See [Table 1](#).

The median number of participants contributing a sample pair across the 154 evaluations was 200 (interquartile range (IQR) 94 to 400) and the median number of SARS-CoV-2 confirmed samples per evaluation was 46 (IQR 25 to 77). The median prevalence (defined as a positive test result on any one sample in a sample pair comparison) across all evaluations was 23% (IQR 13% to 40%). Median prevalence was lowest in oral swab evaluations (14%), 18% in nasal evaluations, 23% in combined oropharyngeal/nasal evaluations, 25% in gargle evaluations, 26% in oral rinse evaluations, 28% in saliva evaluations, and 37% in oropharyngeal evaluations. The difference in median prevalence across evaluations is not obviously explained by differences in the distribution of setting across index test evaluations. See [Table 2](#), [Table 3](#) and [Table 4](#).

Participants may contribute more than one sample pair per participant cohort, but study participants contributed only one sample pair per analysis except for eight evaluation cohorts: [Tu 2020 \[A\]](#) and [Tu 2020 \[B\]](#) contributed anterior and mid-turbinate nasal samples to the overall quantitative analysis of nasal samples ([Figure 6](#)); [Mestdagh 2021 \(a\)\[A\]](#), [Mestdagh 2021 \(a\)\[B\]](#), [Mestdagh 2021 \(d\)\[A\]](#) and [Mestdagh 2021 \(d\)\[B\]](#) both contributed saliva spit and saliva salivate to the overall quantitative analysis of saliva samples ([Figure 7](#)); and [Abdollahi 2020a](#) and [Abdollahi 2020b](#) contributed self-collected oropharyngeal and self-collected nasopharyngeal samples to the narrative synthesis of the "operator" subgroup of evaluations (see [Figure 8](#)).

Figure 6. Forest plot: nasal by COVID-19 test technology and collection method *Footnotes*

Ag: antigen; **CI:** confidence interval; **COVID-19:** coronavirus disease 2019; **N/A:** not applicable; **nos:** not otherwise specified; **PCR:** reverse transcription polymerase chain reaction; **tech:** technology

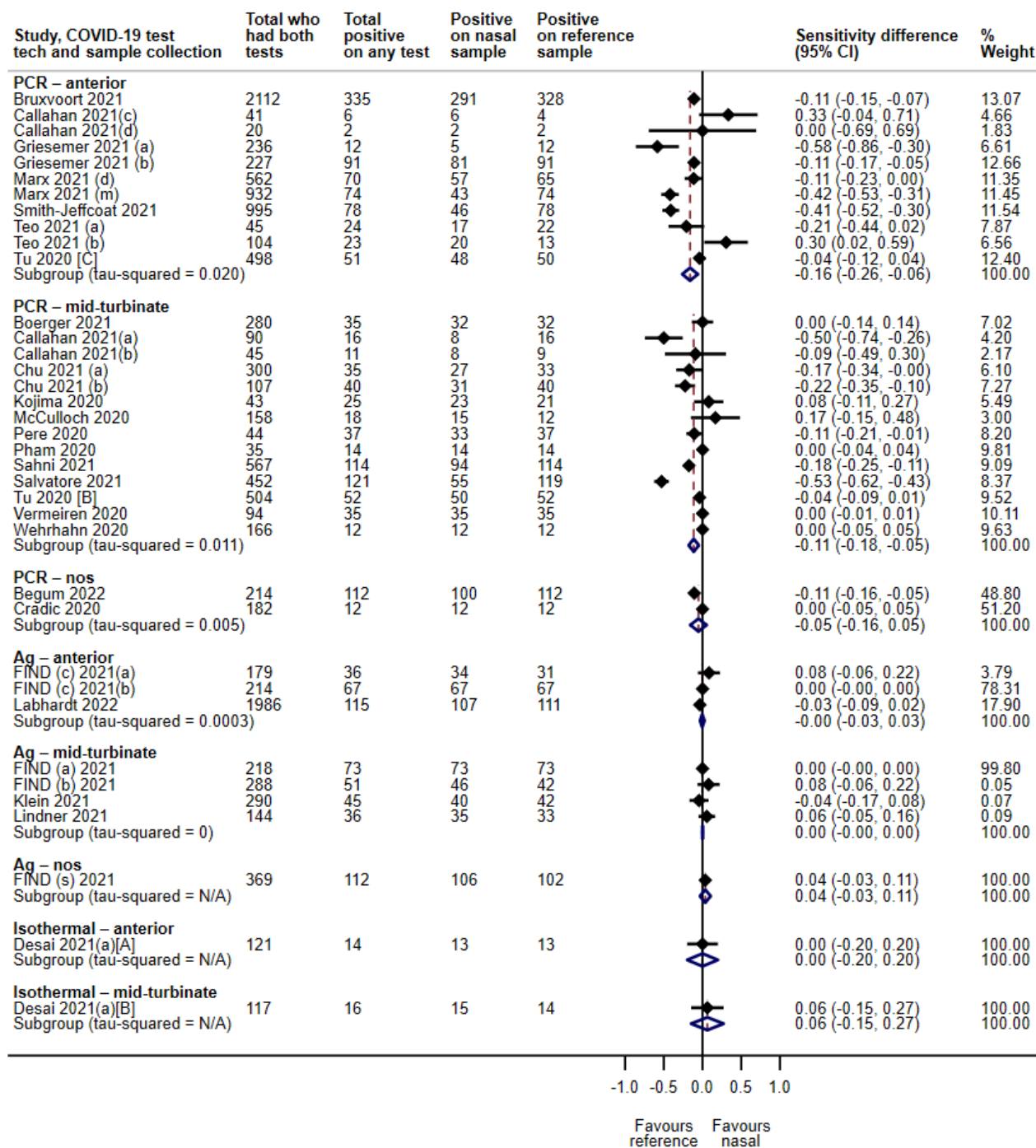


Figure 7. Forest plot: saliva by collection method *Footnotes*

CI: confidence interval; COVID-19: coronavirus disease 19; N/A: not applicable; nos: not otherwise specified; PCR: reverse transcription polymerase chain reaction; TMA: transcription-mediated amplification

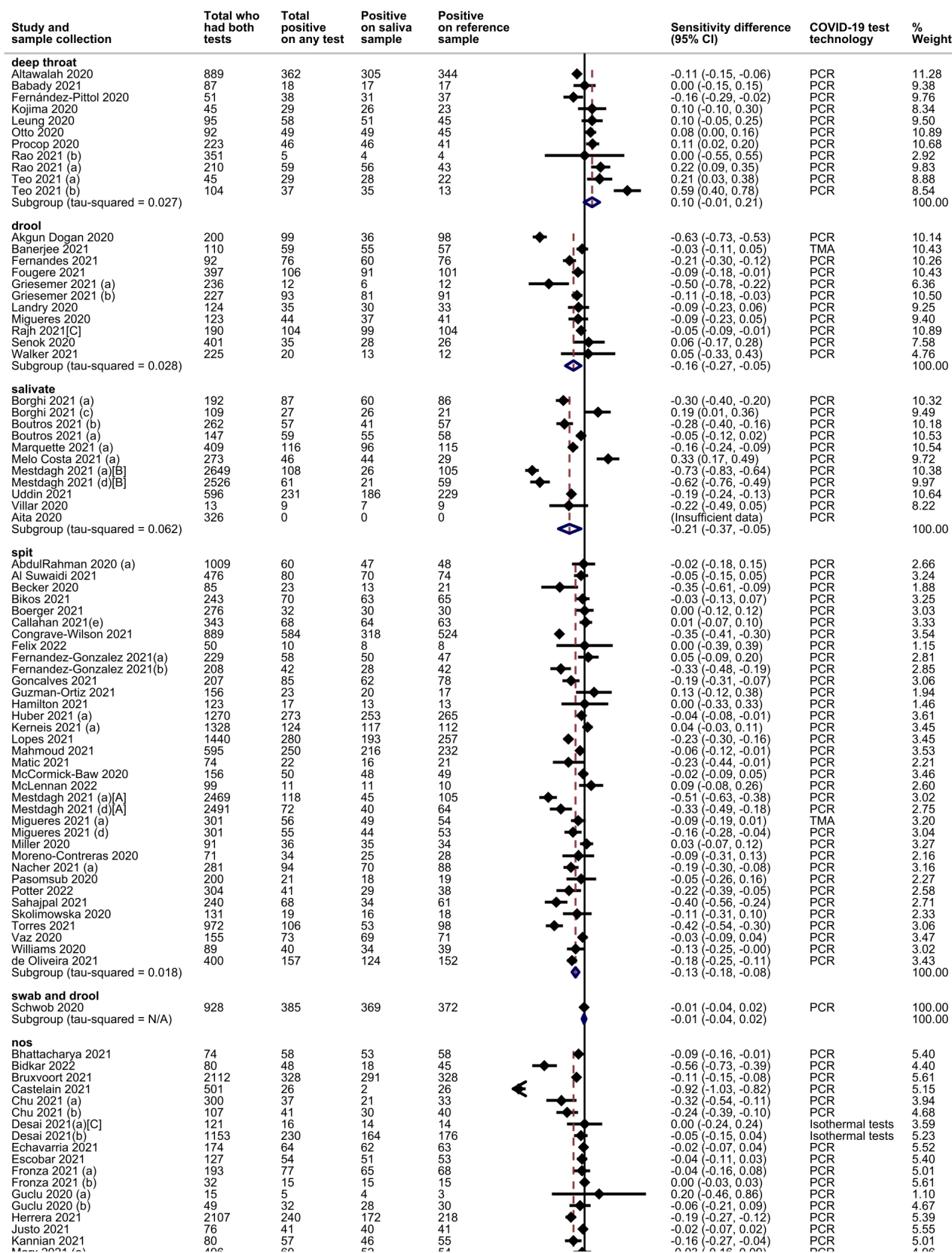
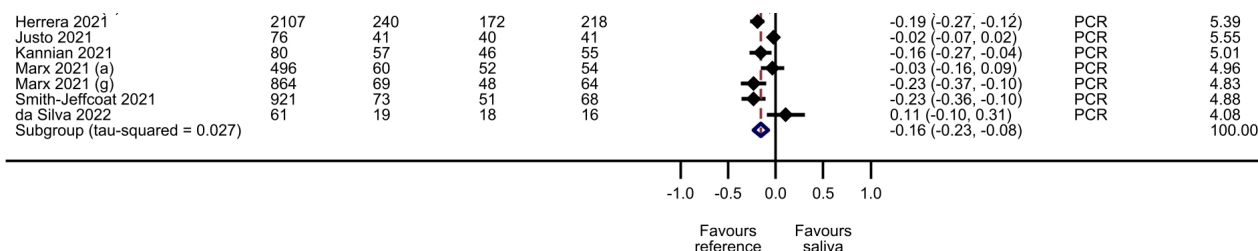
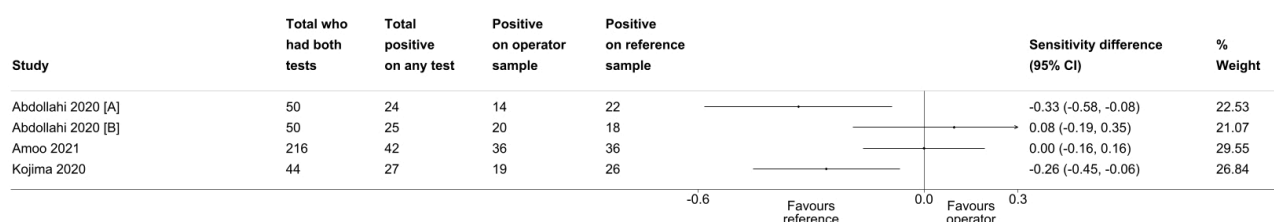


Figure 7. (Continued)

Figure 8. Forest plot: operator *Footnotes*
CI: confidence interval

Results are presented as the difference in sensitivity between index and reference samples. The index sample is the sample under evaluation; one of saliva, nasal, oropharyngeal, nasal/oropharyngeal, gargle or oral. The reference sample is a nasopharyngeal sample in 134/154 (87%) evaluation cohorts and a combined oropharyngeal/nasopharyngeal sample in 20 (13%) evaluation cohorts. For ease, we refer to the reference sample as a "nasopharyngeal" sample (see: Table 2; Table 3; Table 4). If the reported difference in sensitivity is negative, the index sample misses more cases of SARS-CoV-2 infection compared to a nasopharyngeal sample. If the difference in sensitivity is positive, more cases of SARS-CoV-2 infection (true positives (TP)) are detected by the index sample compared to the nasopharyngeal sample.

Indeterminate results were classified as positive for the purposes of our analysis. Indeterminate results were reported for 13 of 154 (8%) evaluations. Most (9/13, 69%) evaluations reporting indeterminate results were in saliva samples (proportion indeterminate index sample results < 1% (Herrera 2021) to 9.4% (Becker 2020)), two were in gargle samples (< 1% (Fernandez-Gonzalez 2021 (c)) to 2.7% (Dumaresq 2021)) and one each in oral samples (1.3%; Goncalves 2021) and nasal samples (2.5%; McCulloch 2020).

Sensitivity of sample types across different SARS-CoV-2 test technologies

See Table 1.

The included studies used a variety of CoV-2 test technologies. RT-PCR was used for most (140/154, 91%) evaluations. The remaining evaluations used: isothermal techniques (2/90, 2% of saliva sample evaluations and 2/37, 5% nasal sample evaluations); transcription-mediated amplification (TMA) (2/90, 2% of saliva sample evaluations) or AG-RDTs (8/37, 22% of nasal sample evaluations). Prior to investigating the accuracy of different sample types and variation in operator expertise combining studies that

used different testing technologies, it was necessary to investigate whether performance of different sample types varied across different types of molecular test (RT-PCR, TMA and isothermal tests).

There was no evidence that the sensitivity of saliva samples (compared to a nasopharyngeal sample) varied across the three subgroups of molecular testing technologies: RT-PCR, isothermal tests or TMA (see Table 1; figure 12, figure 13 and figure 14 in Appendix 8). Due to the small number of evaluations and lack of evidence for a difference in sensitivity in alternatives to RT-PCR in the saliva evaluations, we did not differentiate between test technology for investigations of heterogeneity in the saliva group of studies.

Within the nasal group of evaluations (mid-turbinate and anterior collection methods combined), there was no evidence that the sensitivity of nasal samples (compared to a nasopharyngeal sample) differed when used with RT-PCR or with isothermal tests. Eight nasal evaluations (four with mid-turbinate and two with anterior collection) contributed to the Ag-RDT analysis. There was borderline evidence that the sensitivity of nasal samples (compared to nasopharyngeal samples) was different in AG-RDTs compared to molecular testing technologies (RT-PCR and isothermal tests); see Table 1 and Figure 6. However, except for the investigation of sensitivity according to anterior and mid-turbinate sample collection (reported below), data were too sparse to undertake the majority of investigations of heterogeneity in the nasal sample AG-RDT subgroup (see Appendix 9).

Sensitivity of different sample types for the detection of SARS-CoV-2 infection with molecular tests (RT-PCR, TMA and isothermal tests)

See Table 1 and Figure 6, Figure 7, Figure 8, Figure 9, Figure 10, Figure 11 and Figure 12.

Figure 9. Forest plot: Oropharyngeal Footnotes
CI: confidence interval; OP: oropharyngeal

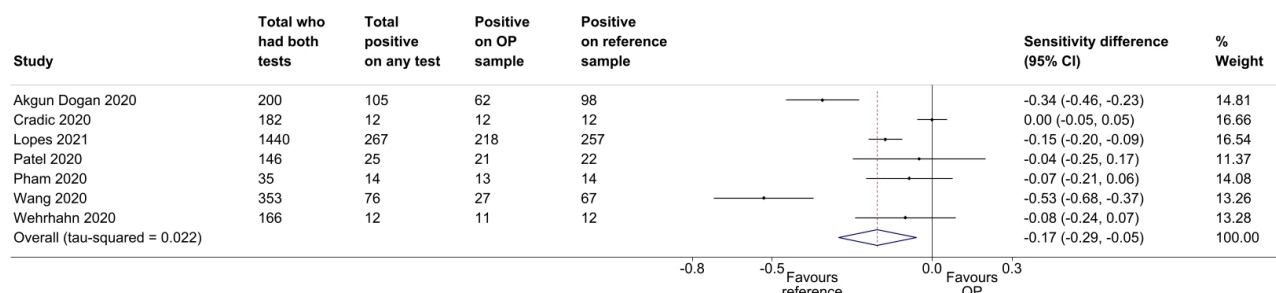


Figure 10. Forest plot: gargle Footnotes
CI: confidence interval

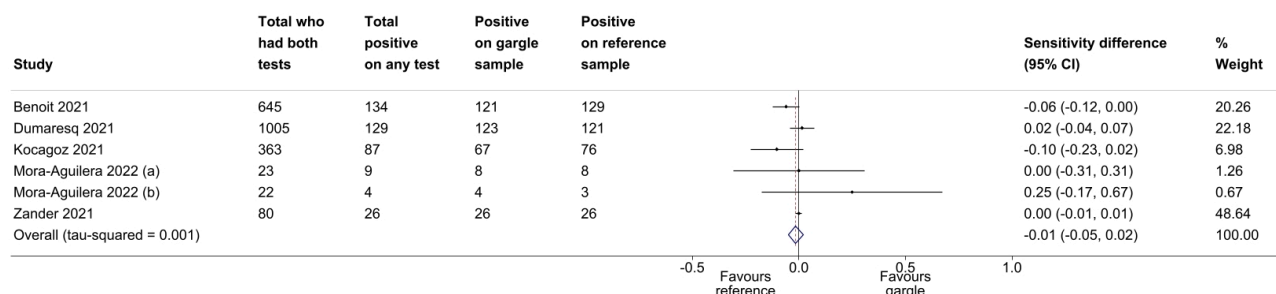


Figure 11. Forest plot: nasal/oropharyngeal Footnotes
CI: confidence interval; Nasal/OP: nasal/oropharyngeal combined sample

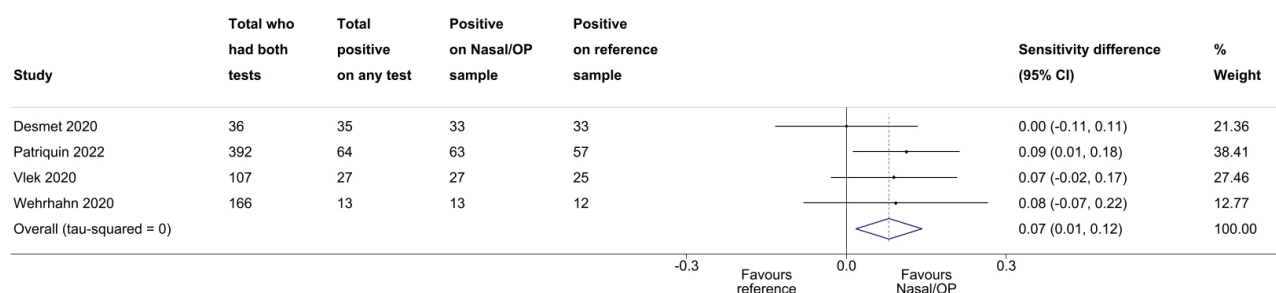
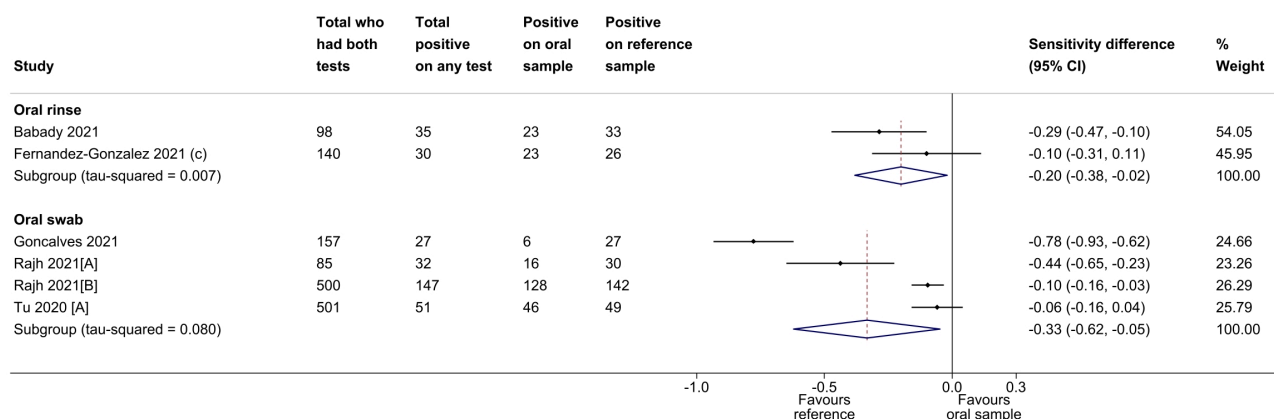


Figure 12. Forest plot: oral Footnotes
CI: confidence interval

Compared to a nasopharyngeal sample, there was evidence for a higher sensitivity of nasal/oropharyngeal samples combined in the same sample container (sensitivity difference +7 percentage points, 95% CI +1 to +12; based on four evaluations, 701 sample pairs including 139 with confirmed SARS-CoV-2).

Compared to a nasopharyngeal sample, there was no evidence of a difference in sensitivity for:

- Gargle samples (sensitivity difference -1 percentage points, 95% CI -5 to +2; based on six evaluations, 2138 sample pairs including 389 with confirmed SARS-CoV-2);
- Deep throat saliva samples (sensitivity difference +10 percentage points, 95% CI -1 to +21; based on 11 evaluations, 2192 sample pairs including 730 with confirmed SARS-CoV-2);
- Saliva collected using a combination of swabbing and drooling (sensitivity difference -1 percentage point, 95% CI -4 to +2; based on one evaluation, 928 sample pairs including 385 with confirmed SARS-CoV-2).

Compared to a nasopharyngeal sample, there was evidence for a lower sensitivity in descending order of the following sample types.

- Oral swab samples (sensitivity difference -33 percentage points, 95% CI -62 to -5; based on four evaluations, 1243 sample pairs including 257 with confirmed SARS-CoV-2);
- Oral rinse samples (sensitivity difference -20 percentage points, 95% CI -38 to -2; based on two evaluations, 238 sample pairs including 65 with confirmed SARS-CoV-2);
- Oropharyngeal samples (sensitivity difference -17 percentage points, 95% CI -29 to -5; based on seven evaluations, 2522 sample pairs including 511 with confirmed SARS-CoV-2);
- Saliva samples collected using spitting, drooling or salivating (sensitivity difference on average -12 percentage points, 95% CI -16 to -8, based on 56 evaluations, 27,253 sample pairs including 4636 with confirmed SARS-CoV-2). We did not find any evidence of a difference in the sensitivity of saliva collected using spitting, drooling or salivating (sensitivity difference ranges from -13 percentage points (spit) to -21 percentage points (salivate));
- Nasal samples (mid-turbinate, anterior nares and unclear collection method combined) (sensitivity difference -12 percentage points, 95% CI -17 to -7; based on 29 evaluations, 9291 sample pairs including 1485 with confirmed SARS-CoV-2).

We did not find any evidence of a difference in sensitivity between nasal samples from these two collection sites with RT-PCR.

Sensitivity of nasal samples for the detection of SARS-CoV-2 infection with rapid antigen tests

See [Table 1](#) and [Figure 6](#).

Compared to a nasopharyngeal sample, there was no evidence for a difference in sensitivity of nasal samples when used with AG-RDTs (sensitivity difference 0 percentage points, 95% CI -0.02 to +0.02; based on eight evaluation cohorts, 3688 sample pairs including 535 with confirmed SARS-CoV-2). Compared to a nasopharyngeal sample, there was no evidence of a difference in sensitivity between nasal samples collected from the mid-turbinates or from the anterior nares in rapid antigen tests.

The effect of sample operator expertise on the sensitivity of sample types for the detection of SARS-CoV-2 infection

See [Figure 8](#).

Two evaluations concerned the effect of operator expertise on the collection of nasopharyngeal samples. One evaluation demonstrated a reduction in sensitivity with self-collection compared to healthcare worker (HCW) collection (sensitivity difference -33 percentage points, 95% CI -58 to -8; based on 50 sample pairs including 24 with confirmed SARS-CoV-2; [Abdollahi 2020a](#)) and the other found no evidence of a difference in sensitivity with self-collection compared to HCW collection (sensitivity difference 0 percentage points, 95% CI -16 to +16; based on 216 sample pairs including 42 with confirmed SARS-CoV-2; [Amoo 2021](#)).

One evaluation assessed the effect of operator expertise on the collection of oropharyngeal samples and demonstrated no evidence of a difference in sensitivity with self-collection compared to HCW collection (sensitivity difference -8 percentage points, 95% CI -19 to +35; based on 50 sample pairs including 25 with confirmed SARS-CoV-2; [Abdollahi 2020b](#)).

One evaluation cohort assessed the effect of operator expertise on the collection of saliva samples and demonstrated a reduction in sensitivity of self-collection compared to supervised (by HCW) self-collection (sensitivity difference -26 percentage points, 95% CI -45

to -6; based on 44 sample pairs including 27 with confirmed SARS-CoV-2; [Kojima 2020](#)).

Investigations of heterogeneity

For gargle samples, oral rinse samples, oral swab samples, oropharyngeal and combined nasal/oropharyngeal samples and operator experience, we were not able to undertake any planned investigations of heterogeneity because of sparse data.

For saliva studies, we investigated the effect of participant age, symptom status, and operator (HCW, self-collection or supervised self-collection) on sensitivity compared to a nasopharyngeal sample for all saliva collection methods combined and within subgroups of different saliva collection methods. Due to sparse data, we were only able to investigate the effect of the use of transport media and time of sample collection in relation to symptom onset for all saliva collection methods combined.

For nasal samples, we were able to investigate the effect of symptom status, time of sample collection, use of transport media and operator expertise (HCW or self collection) on sensitivity compared to a nasopharyngeal sample for all nasal collection methods combined and in molecular and antigen tests combined.

Saliva samples

We observed a lower sensitivity in HCW collected compared to self-collected (sensitivity difference -9 percentage points, 95% CI -13 to -6; based on 21,984 sample pairs including 5209 with confirmed SARS-CoV-2) and HCW-collected compared to supervised self-collected (sensitivity difference -14 percentage points, 95% CI -22 to -6; based on 17,251 sample pairs including 2028 with confirmed SARS-CoV-2) subgroups in the saliva group of studies. However, this result should be interpreted with caution as the single HCW-collected saliva evaluation in this comparison is an outlier: [Castelain 2021](#) (sensitivity difference -92 percentage points, 95% CI -103 to -82; based on 501 sample pairs including 26 with confirmed SARS-CoV-2). See [Appendix 10](#) and [Appendix 11](#).

We did not observe evidence of a difference in sensitivity for saliva samples (all collection methods combined or within collection method subgroups) compared to a nasopharyngeal sample beyond that expected by chance according to age (adult versus child) or symptom status (symptomatic versus asymptomatic). We did not observe evidence of a difference in sensitivity for saliva samples (all collection methods combined) by the time of post-symptom onset (≤ 1 week post-symptom onset, ≤ 2 weeks post-symptom onset and ≤ 3 weeks post-symptom onset) or use of transport medium (transport medium versus no transport medium) beyond that expected by chance. See [Appendix 8](#) and [Appendix 10](#).

Nasal samples

We observed a reduction in sensitivity of nasal samples compared to a reference sample greater than would be expected by chance with increasing time post-symptom onset: ≤ 1 week post-symptom onset (-2 percentage points, 95% CI -3 to -0.3; based on 6764 sample pairs including 1077 with confirmed SARS-CoV-2); ≤ 2 weeks post-symptom onset (-13 percentage points, 95% CI -23 to -2; based on 1808 sample pairs including 240 with confirmed SARS-CoV-2) and ≤ 3 weeks post-symptom onset (-46 percentage points, 95% CI -96 to -4; based on 569 sample pairs including 149 with confirmed SARS-CoV-2). See [Appendix 8](#) and [Appendix 11](#).

We did not observe evidence of a difference in sensitivity beyond that expected by chance for nasal samples in molecular and AG-RDTs combined (all collection methods combined or within collection method subgroups (anterior and mid-turbinate)) compared to a nasopharyngeal sample by symptom status (symptomatic versus asymptomatic), use of transport medium (transport medium versus no transport medium) or operator expertise (HCW versus self-collection).

Sensitivity analysis

We undertook a sensitivity analysis comparing the main analyses (which included evaluations where the kit manufacturer or components of a testing kit differed across two samples in a pair) with analyses where these evaluations were removed (10 evaluations of saliva samples, five evaluations of nasal samples, two evaluations of oral swabs and one evaluation of gargle samples). We also undertook sensitivity analysis comparing the main analyses (corrections applied to studies with zero variance allowing those studies to be included in the pooled estimates) and analyses eliminating studies with a within-study variance of the sensitivity difference equal to zero (10 evaluations of nasal samples, one evaluation of saliva samples, one evaluation of oropharyngeal samples, and one evaluation of gargle samples).

Our conclusions were not changed by the results of the sensitivity analyses ([Appendix 12](#)).

DISCUSSION

This review summarises evidence from within-person (direct) comparisons of the sensitivity of alternative sample sites (compared to nasopharyngeal samples) and the effect of operator expertise on the detection of SARS-CoV-2 in ambulatory populations. The results of this review are based on published journal articles or studies available as preprints from 1 January 2020 up until 22 February 2022. In addition, we also included evaluations that were available as independent, national reference laboratory publications or that were co-ordinated and published by FIND, and journal articles that were listed on the Diagnostics Global Health website until 30 April 2021.

Summary of main results

We included data from 106 studies reporting 154 evaluations, with a total of 60,523 sample pairs (participants) and 11,045 participants with confirmed SARS-CoV-2.

The key findings are presented in [Summary of findings 1](#).

We summarise nine key findings from this review below.

1. There is no evidence that the sensitivity of gargle samples or deep throat saliva samples differs from nasopharyngeal samples when used with RT-PCR.

There is no evidence of a difference in sensitivity of gargle samples or deep throat saliva samples compared to nasopharyngeal samples for the detection of SARS-CoV-2 with RT-PCR. There is evidence from one study that saliva collected using a combination of swabbing and drooling has a comparable sensitivity to nasopharyngeal samples for the detection of SARS-CoV-2 with RT-PCR. Considerable heterogeneity exists in the evidence base for gargle samples and deep throat saliva.

2. There is some evidence that combined oropharyngeal/nasal samples demonstrate a higher sensitivity than nasopharyngeal samples when used with RT-PCR.

There is some evidence that combined oropharyngeal/nasal samples demonstrate higher sensitivity (average +7% percentage points) compared to a nasopharyngeal sample. However, this finding is based on only four evaluations (701 sample pairs) and collection methods varied (for example, two of the four evaluation samples were collected by healthcare workers, one was self-collected, and in one evaluation this was not stated).

3. Nasal (anterior nares and mid-turbinate), saliva (spit, drool, salivate), oropharyngeal and oral samples demonstrate a reduction in sensitivity compared to nasopharyngeal samples when used with RT-PCR.

Nasal, saliva (spit or salivate or drool), oropharyngeal and oral samples demonstrate a reduction in sensitivity compared to nasopharyngeal samples in descending order from oral swabs (average of 33% percentage points lower), oral rinse samples (20 percentage points lower), oropharyngeal samples (17 percentage points lower), saliva (spit or drool or salivate) samples (12 percentage points lower) and nasal (anterior or mid-turbinate) samples (12 percentage points lower). Formal, indirect statistical comparison of sensitivities by sample site were not undertaken due to substantial heterogeneity and potential confounding. Overlapping 95% confidence intervals for the summary sensitivities suggest no evidence of a difference in sensitivity between these sample types, but for oral and oropharyngeal samples, the number of evaluations is small and there is substantial imprecision in estimates.

4. There is no evidence that the sensitivity of nasal samples (anterior or mid-turbinate) differs from nasopharyngeal samples when used with Ag-RDTs, but the applicability of this finding to self-testing is unclear.

Evidence for the accuracy of different sample types used with rapid antigen tests was limited in our review. In eight evaluations, there was no evidence of a difference in sensitivity of nasal samples compared to nasopharyngeal samples when used with rapid antigen tests. Only three of five evaluations of Ag-RDTs documented collection methods and, in these three evaluations, the sample was interpreted by a healthcare professional or self-collected and interpreted whilst supervised by a healthcare professional. It is therefore unclear the extent to which estimates of sample sensitivity for use with rapid antigen tests represent self-sampling, self-testing or healthcare worker testing.

5. There is no evidence that the sensitivity of saliva samples changes with increasing time post-symptom onset.

We did not find any evidence that the sensitivity of saliva samples differed with time post-symptom onset, but conclusions are limited by the relatively small number of studies ≥ 3 weeks post-symptom onset. In nasal samples, sensitivity decreased with time, from minus two percentage points at one week post-symptom onset to -46 percentage points at three weeks post-symptom onset compared to nasopharyngeal samples. The finding of a decline in sensitivity over time in nasal samples is in line with existing evidence (Mallett 2020; Weiss 2020; Wolfel 2020). The lack of a decline in the sensitivity of saliva samples (all collection methods combined) over time may be a reflection of the presence of

secretions from the lower respiratory tract in deep throat saliva. Viral load has been shown to decrease more slowly in the lower respiratory tract compared to the upper respiratory tract (Mallett 2020; Weiss 2020).

6. Poor reporting hampers quality assessment.

Only 3% of included evaluations were at low risk of bias overall. However, poor reporting precluded reliable quality assessment. Most evaluations were judged as having unclear risk of bias (59% in the flow and timing domain, 74% in the participant domain and 77% in the index test domain). Where risk of bias assessment was possible, methodological concerns included enrichment of cohorts with confirmed SARS-CoV-2-positive participants, inappropriate exclusions (for example, because of an inability to collect sufficient sample volume), lack of blinding between samples being compared, non-random ordering of samples being compared, and incomplete recording and/or analysis of excluded, lost or invalid samples. Similarly, poor reporting precluded assessment of applicability in the participant (77%) and index test (38%) domains. In particular, only 38% of evaluation cohorts reported time of testing with reference to symptom onset in symptomatic participants, which may confound results, particularly in index groups or subgroups containing few evaluations. The most likely impact of confounding in this review will be to undermine our assessment of the relative sensitivity of different collection methods and of different anatomical sampling sites relative to one another.

7. Poor reporting and sparse data limited investigations of heterogeneity.

Age, symptom status and use of transport media do not appear to affect the sensitivity of saliva and nasal samples.

We were limited by sparse data and were only able to perform some of our planned investigations of heterogeneity in saliva and nasal samples. We did not find any difference in sensitivity according to age or symptom status for any sample type, although the number of evaluations in children (saliva 6/90, 6.4%) and nasal (1/37, 2.7%), respectively, and in asymptomatic participants (saliva 6/90, 6.7%) and nasal (1/37, 2.7%), respectively, was relatively small. We did not find any evidence that the use of transport media affected the sensitivity of saliva samples or nasal samples. For nasal samples, the number of evaluations without transport media was small (7/37, 18.8%) and so the implications of this finding are unclear. However, for saliva samples, approximately half the total number of evaluations were performed without transport media (42/90, 46.7%), which increases our certainty in this finding.

The effect of operator expertise on the sensitivity of samples is unclear.

We only identified four evaluations that investigated the effect of operator expertise on the sensitivity of samples, and our ability to investigate operator expertise as a source of heterogeneity in this review was limited by lack of reporting and sparse data. Findings are conflicting, and where we had evidence, we found no consistent effect of operator expertise on the sensitivity of nasopharyngeal, oropharyngeal, nasal or saliva samples when used with RT-PCR. Data were too sparse to investigate the effect of operator experience on the sensitivity of nasal samples in Ag-RDTs.

8. Most of the evidence about alternatives to nasopharyngeal swabs has been conducted with RT-PCR and concerns self-sampling.

Most (146, 95%) evaluations were conducted with molecular tests and, of these, 140 (91%) were conducted with RT-PCR. Only eight evaluations using nasal samples were conducted with Ag-RDTs.

Many of the index samples used for molecular tests were self-collected (57%) or self-collected whilst supervised by a healthcare professional (23%). Most of the evaluations of samples for use with RT-PCR in this review, therefore, relate to self-sampling.

9. Evidence about the sensitivity of different sample types is lacking in children and in asymptomatic populations.

Median SARS-CoV-2 prevalence across evaluation cohorts was 23%. Twenty-eight of 154 evaluations were conducted in mixed populations but only seven (5%) evaluations were conducted on children. This is particularly important given that most of the samples in this review were self-collected. The accuracy of samples reported in this review may not be replicable in children.

Many evaluations were conducted in dedicated COVID-19 testing clinics or in ambulatory hospital settings (55%). Testing in the context of targeted screening or contact tracing accounted for only 4% of evaluations. This is reflected by the fact that 46% of evaluations were conducted in mixed symptomatic and asymptomatic populations, whilst only seven (5%) were conducted in asymptomatic populations. We were not able to demonstrate any effect of symptom status on the sensitivity of different sample types in this review, which may point to our findings being applicable in symptomatic and asymptomatic populations. Alternatively, the lack of an effect of symptom status in this body of evidence may be an artefact as a result of the relatively low number of asymptomatic evaluation cohorts contributing to this subgroup analysis.

Illustration of predicted effect of testing by sample type

Assuming that missed cases of SARS-CoV-2 occur solely on the basis of a difference in sensitivity as a result of variation in the sample collection method and applying our results (where evidence is available from more than five studies) to a cohort of 1000 people with SARS-CoV-2, in whom 230 people had confirmed infection (median prevalence of 23% in included evaluations in our review), compared to a nasopharyngeal or combined oropharyngeal/nasopharyngeal sample, we estimated the following:

With RT-PCR

- There would be *no difference* in the number of cases of SARS-CoV-2 infection detected with gargle samples -2 (-12 to +5) or with saliva samples collected from the deep throat -23 (-2 to +48);
- Using nasal samples collected either from the anterior nares or mid-turbinate, on average, 28 (-16 to -39) fewer cases of SARS-CoV-2 infection would be detected;
- Using saliva samples collected by spitting, on average, 30 (-18 to -41); with drooling, on average, 37 (-12 to -62); and with salivating, on average, 48 (-12 to -85) fewer cases of SARS-CoV-2 infection would be detected;
- Using oropharyngeal samples, 39 (-12 to -67) fewer cases of SARS-CoV-2 infection would be detected.

With Ag-RDTs

Assuming missed cases of SARS-CoV-2 occur solely on the basis of a difference in sensitivity as a result of variation in sample collection method, compared to a nasopharyngeal or combined oropharyngeal/nasopharyngeal sample, we estimated:

- Using nasal samples (anterior or mid-turbinate), there would be *no difference*: 0 (0 to 0) in the number of cases of SARS-CoV-2 infection detected.

Strengths and weaknesses of the review

To our knowledge, this is the most up-to-date and comprehensive summary of the evidence for the sensitivity of different sample sites and collection processes for the detection of SARS-CoV-2, based on within-person (direct) comparisons. Our review results have increased certainty in, and are broadly consistent with, existing systematic reviews with respect to nasal/oropharyngeal (Lee 2021), deep throat saliva (Butler-Laporte 2021) and gargle (Tsang 2022) achieving the highest sensitivities compared to nasopharyngeal samples. Oropharyngeal, undifferentiated saliva and undifferentiated nasal sample sensitivities were between 12 and 18 percentage points lower than nasopharyngeal samples when used with RT-PCR (Atieh 2021; Bastos 2021; Butler-Laporte 2021; Kivela 2021; Lee 2021). In addition, this review has been able to examine the sensitivity of alternative nasal (anterior nares and mid-turbinate) samples and saliva (salivate, swab and drool) collection techniques, the sensitivity of oral samples and the effect of operator expertise on sensitivity. Due to a larger body of evidence, compared to previous reviews, we have been able to investigate the effect of symptom status, age, use of transport media and time post-symptom onset on the sensitivity of nasal and saliva sample types. This review also presents within-person evidence for the sensitivity difference of nasal compared to nasopharyngeal samples for use with Ag-RDTs.

Our review used a broad search, screening all articles concerning COVID-19 or SARS-CoV-2. We undertook all screening and eligibility assessments, QUADAS-2 (Whiting 2011) and QUADAS-C (Yang 2021) assessments, and data extraction of study findings independently and in duplicate. Although it is possible that the use of artificial intelligence text analysis to identify studies most relevant to diagnostic questions may have led to some eligible studies being missed, we believe that the multi-stranded search strategy used will have identified most, if not all, relevant literature. We have reasonable confidence in the completeness and accuracy of the findings up until the search date.

The robustness of our findings depends on the quality of the sample pair comparisons. To this end, we restricted inclusion to within-person comparison of sample pairs in participants suspected of having SARS-CoV-2 infection at the time of testing, with both sample types included in the comparison. We excluded studies where participants were exclusively preselected for inclusion based on being known as SARS-CoV-2-positive in the reference sample. We further restricted studies to those where the samples being compared were collected within the same clinical encounter, excluding studies where time between collection of different sample types was reported as being longer than 24 hours. We undertook quality assessment of the sample pair comparison using items from the QUADAS-C checklist for comparative diagnostic test accuracy studies (Yang 2021), interrogating included studies

for comparability of the sampling process (for example, operator skill, unless this was the sampling variable being compared), extraction process, type of SARS-CoV-2 test, gene targets, and disease positivity threshold. We also assessed included studies for bias that may be introduced by the order in which samples were taken (for example, comparison of oropharyngeal samples with nasopharyngeal/oropharyngeal samples and nasal samples with nasopharyngeal samples).

The analytical approach to this review precludes estimation of specificity. We consider that the occurrence of false positives would be negligible for molecular and antigen-based tests (Dinnes 2022) and similar between sample sites. We assume that the impact of false negatives from the testing technology (molecular or antigen in this review) on the validity of estimates of differences in sensitivity will be minimised, provided the testing method is the same for each sample in a pair and assuming that false negatives from different sample types are not independent. The validity of our estimates of the comparative sensitivity of sample pairs, therefore, depends on the assumption that differences in false negatives arise only as a result of differences in the sample type or process being investigated, rather than other elements of the sampling and testing process. In 141/154 (92%) sample pair comparisons, the same extraction and testing kits were used for each sample in a pair. For 13 sample pair comparisons (7/90 saliva samples, 3/37 nasal samples, 2/6 oral samples and 1/7 oropharyngeal samples), extraction and/or testing were undertaken using the same method but different testing kits for each sample in a pair. A sensitivity analysis in affected index tests did not demonstrate an effect of differences in the testing process on estimates of sensitivity.

The main limitations of this review arise as a result of limitations in the evidence base. Poor reporting of the sampling process itself, such as the order in which samples were collected and blinding of interpretation between index and reference samples in 77% of included evaluations, undermined a comprehensive assessment of the validity of sample comparisons. Except for saliva and nasal samples, the number of studies contributing to accuracy estimates was small, reducing our confidence in the reliability of our findings and precluding planned investigations of heterogeneity in oropharyngeal, combined nasal/oropharyngeal, gargle and oral samples. The number of evaluations in Ag-RDTs was small and was restricted to evaluations of nasal samples. Poor reporting hampered a comprehensive assessment of methodological quality and applicability and further undermined investigations of heterogeneity. In 62% of evaluations, the time of sampling in relation to symptom onset was not stated.

Most of the included studies did not report the occurrence or management of indeterminate results, which precluded sensitivity analysis investigating the effect of these on estimates of accuracy or commenting on the effect of this on the clinical utility of different sample types. Our approach to analysis of studies where indeterminate results were reported was to classify these as 'positive' for estimation of sensitivity. This approach was taken because indeterminate results are more aligned to a positive rather than a negative test result in terms of clinical action and impact on the person tested, and because excluding indeterminate results would have resulted in overestimation of sensitivity. Although our inclusion criteria and (where reported) most (67%) evaluations were undertaken within one week of symptom onset, we cannot rule out the effect of confounding by time since symptom onset on

our comparison of the relative accuracy of different index sample types compared to a nasopharyngeal sample. Despite the search date of this review (22 February 2022), we consider it unlikely that research conducted since the completion of searches would alter the conclusions.

Applicability of findings to the review question

Most (81%) studies recruited participants prospectively on the basis of a suspicion of SARS-CoV-2 infection. Participants were symptomatic (33%) or mixed symptomatic and asymptomatic (46%) and the median prevalence was 23% (IQR 13% to 40%). Most (69%) studies were conducted in dedicated COVID-19 testing centres and community or outpatient settings. Less than 4% of included evaluations were conducted in the context of targeted screening (for example, in school or hospital settings) or as part of contact tracing. Our ability to explore whether the accuracy of samples varied according to symptom status was limited, but did not appear to have an effect on the sensitivity of saliva sample evaluations. The applicability of these findings to asymptomatic, screening populations is unclear.

We aimed to include studies recruiting individuals early in the course of infection. Only one-third of evaluation cohorts (58/154) reported time of testing with reference to symptom onset in symptomatic participants. However, in most of these, 58 evaluation cohorts testing, this was undertaken within one week of symptom onset (67%) and in a minority (10%), up to three weeks post-symptom onset. Our ability to quantify any difference in sensitivity over time post-symptom onset with different sample types was therefore limited. Existing evidence demonstrates superior test performance with upper respiratory tract samples for symptomatic participants in the first 7 to 10 days post-symptom onset (Dinnes 2022; Mallett 2020; Weiss 2020; Wolfel 2020), probably corresponding with higher viral loads (Cevik 2021). We consider that estimates of sensitivity for the majority of (upper respiratory) sample types in this review are likely to be the most optimistic of those possible. Virus is more likely to be detected by lower respiratory tract samples and nonrespiratory tract samples after this time. The finding in this review, that the sensitivity of saliva samples (as a nonrespiratory tract sample) does not appear to decline over time, is compatible with existing research concerned with lower respiratory tract samples (Mallett 2020; Weiss 2020).

In the evaluations conducted with RT-PCR, only seven were conducted on children and most (80%) index samples were self-collected. In the rapid antigen evaluations, none were conducted on children and in the three where this was reported, only one was self-collected whilst being supervised by a healthcare worker (HCW). Our findings for evaluations conducted with RT-PCR are therefore applicable to self-collected samples by adults. For evaluations conducted with rapid antigen tests, it is unclear the extent to which estimates represent healthcare worker testing, self-sampling or self-testing in adults.

AUTHORS' CONCLUSIONS

Implications for practice

This review summarises evidence of the sensitivity of alternative anatomical sample collection sites and collection methods to healthcare worker-collected nasopharyngeal samples for the detection of SARS-CoV-2. Most of the evidence is from symptomatic

adults presenting to dedicated COVID-19 testing centres. Evidence about the sensitivity of sample types in asymptomatic populations and in children is lacking. The implications of this on the applicability of our findings are unclear due to limitations in our investigations of heterogeneity.

For confirmatory testing with NAATs for detection of SARS-CoV-2, the WHO, CDC and ECDC recommend an upper respiratory tract (URT) sample in VTM, with the WHO specifying a combined nasopharyngeal/oropharyngeal specimen (WHO 2020b). CDC recommend saliva as an alternative to URT samples for confirmatory testing with NAATs in symptomatic individuals only when nasopharyngeal samples cannot be collected (Centres for Disease Control 2021), and ECDC recommends saliva only with assays detecting SARS-CoV-2 RNA (ECDC 2021).

There is evidence in this review to suggest that self-collected, combined nasal/oropharyngeal, self-collected gargle samples and self-collected deep throat saliva have comparable sensitivity to healthcare worker-collected nasopharyngeal samples when used with RT-PCR. Self-collected samples have the potential to reduce exposure of healthcare staff to infection and negate the need for Personal Protective Equipment (PPE) with associated resource savings. This review also provides evidence that direct sampling (without the use of transport media) of nasal samples and saliva samples does not result in a decrease in sensitivity. The use of deep throat saliva with RT-PCR, therefore, has, in addition, the potential to save resources and reduce complexity when confirmatory testing is needed at scale. Further, there is evidence from this review that the sensitivity of saliva samples does not appear to decline with increasing time post-symptom onset. This is in contrast to a decline in sensitivity with increasing time post-symptom onset observed with nasal samples in this review, which mirrors the decline in sensitivity with increasing time post-symptom onset observed with URT in other reviews (Mallett 2020; Weiss 2020; Wolfel 2020). This may be an important consideration for choice of sample type in individuals presenting for testing later in the course of the disease.

Self-collected saliva (spit, salivate and drool), nasal (mid-turbinate and anterior nares), oropharyngeal and oral swabs have a lower sensitivity of similar magnitude compared to nasopharyngeal samples when used with RT-PCR. However, the volume of evidence for oropharyngeal and oral samples is relatively small and imprecise. Despite the advantages associated with self-collected compared to healthcare-collected samples, and for saliva and nasal samples, the advantages offered by direct sampling, the reduction in sensitivity compared to healthcare worker-collected nasopharyngeal swabs with these sample types may not be acceptable in testing settings where the purpose of testing is confirmation of SARS-CoV-2 infection.

For rapid antigen tests, WHO, CDC and ECDC recommend URT samples. A limited body of homogenous evidence in this review suggests that nasal samples have comparable accuracy to nasopharyngeal samples when used with rapid antigen tests. Further, we found no evidence for a difference in sensitivity of nasal mid-turbinate and nasal anterior nares samples. This is an important finding for rapid tests as the acceptability of sample collection is likely to be an even more important factor affecting testing uptake in asymptomatic individuals in the community. However, it is unclear in this review the extent to which sensitivity estimates generated from nasal samples used with rapid antigen tests were based on self-collection. These estimates may therefore

not be replicable outside of healthcare settings. We did not find any direct, within-person comparisons of other sample types used with rapid antigen tests. Estimates of the sensitivity of nasal samples used with rapid antigen tests from another review (not restricted to within sample comparisons) in this series suggested a similar sensitivity compared to nasopharyngeal samples (Dinnes 2022). In the same review, saliva samples used with rapid antigen tests had a lower sensitivity compared to nasopharyngeal samples (-36.8 percentage points, 95% CI -43.5 to -30.1).

Where samples have comparable sensitivity and resource implications, the acceptability of the sampling process is an important consideration. Nasal samples have been shown to cause less discomfort than oropharyngeal swabs (Frazee 2018), and research has shown a preference for saliva over nasal samples (McLaughlin 2022). Importantly, in this review, we were not able to demonstrate a difference in sensitivity between nasal mid-turbinate and nasal anterior nares samples, which may have implications for the acceptability of nasal samples. However, acceptability will differ in different population groups. For example, some individuals may struggle to generate a saliva sample (Blackmore 2020). A recent study evaluated the ease of self-collection of direct saliva samples for individuals presenting for SARS-CoV-2 testing, and although 90% of participants perceived saliva collection as simple, one-third of participants had difficulty collecting a sufficient saliva sample volume and 26% of saliva samples required additional processing to reduce viscosity with adverse consequences for laboratory workflow (Plantamura 2021). In this review, indeterminate or invalid results were reported by 40% of saliva evaluation cohorts, 33% of gargle evaluation cohorts and 24% of nasal evaluation cohorts. For saliva, invalid samples were most often a result of inadequate sample volume or because of hyper-viscosity of samples.

Implications for research

Combined nasal/oropharyngeal, gargle samples and deep throat saliva show promise as superior or comparable sample types for use with RT-PCR. More research is needed to increase certainty that these alternative samples can achieve the sensitivity required in settings where confirmation of SARS-CoV-2 infection (with RT-PCR) is the goal of testing.

There is a considerable body of research concerned with the sensitivity of saliva and nasal samples used with RT-PCR in symptomatic and mixed symptom status populations. Evidence for the accuracy of other sample types for use with RT-PCR is lacking. Further research is needed to determine whether oral and oropharyngeal samples have comparable sensitivity to samples where estimates of sensitivity are based on a larger volume of evidence: nasal (anterior and mid-turbinate) and saliva (drool, salivate and spit) samples.

The findings of this review suggest that, in contrast to upper respiratory tract samples, the sensitivity of saliva samples may not decrease as rapidly with increasing time post-symptom onset. Viral load is likely to be higher in symptomatic populations, and it has been demonstrated that virus is cleared more rapidly from samples from children (Weiss 2020). Children and asymptomatic individuals were under-represented in this review. More research is needed to determine whether this finding in predominantly adult, symptomatic individuals is replicable in child and asymptomatic

populations within different saliva collection methods and in testing technologies other than RT-PCR.

Evidence about the sensitivity of different sample types in asymptomatic populations and in children is lacking. This may be a reflection of the lack of evidence for the effect of different sample types and operator experience for the detection of SARS-CoV-2 with rapid antigen tests. Although there is evidence from this review that nasal (anterior or mid-turbinate) samples have comparable sensitivity to nasopharyngeal samples with rapid antigen tests, poor reporting means it is unclear the extent to which this represents healthcare-worker testing, self-sampling or self-testing. The lack of evaluations of different samples and factors that might affect the accuracy of sample collection and interpretation in testing technologies other than RT-PCR is an important omission given the important role of rapid antigen self-testing in pandemic and epidemic settings.

Poor reporting precluded adequate quality assessment and assessment of applicability for evidence in this review; just over half (62%) of samples provided sufficient information to allow replication of sample collection. Similarly, only 31% of evaluation cohorts (48/154) reported invalid and uninterpretable results. Future within-person evaluations should recruit a consecutive sample of participants and provide information about age, time of testing in relation to symptom onset, and exposure. Sampling (and interpretation of rapid antigen tests) procedure should be detailed, including any instruction or training of sample collectors, extraction and testing kits used, and thresholds should be documented. To minimise bias in sample comparisons, authors should carefully consider the potential for contamination of different sample types when deciding on sample order, or randomise the order of sample collection. Interpretation of test results for each sample type should be conducted blind to other sample results. Eligibility and exclusion decisions (including test failures) throughout the whole diagnostic pathway should conform to the updated Standards for Reporting of Diagnostic Accuracy (STARD) guidelines (Bossuyt 2015).

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Editorial and peer-reviewer contributions

The following people conducted the editorial process for this article:

- Sign-off Editor (final editorial decision): Prof Michael D Brown, Emergency Medicine, Michigan State University College of Human Medicine; and Dr Mia Schmidt-Hansen, National Institute for Health and Care Excellence, London, United Kingdom;
- Managing Editor: Joanne Duffield, Cochrane Central Editorial Service (selected peer reviewers, provided editorial guidance to authors, edited the article); and Sophie Beese, Research Fellow, Biostatistics, Evidence Synthesis, Test Evaluation and Modelling, Institute of Applied Health Research, University of Birmingham, Edgbaston (selected peer reviewers, provided editorial guidance to authors);
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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Abdollahi 2020a

Study characteristics

Patient Sampling	Single-group study to estimate agreement between technician and self-collected nasopharyngeal and oropharyngeal samples for detection of Sars-CoV Design: 50 (28) adult patients with clinical and radiologic evidence of viral pneumonia admitted to an infectious diseases ward Recruitment: Random Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Inpatient Location: Imam Khomeini Hospital Complex, Tehran Country: Iran Dates: February 28 to April 27, 2020 Symptoms and severity: Fever: 34 (68%) Muscle pain: 30 (60%) Cough: 30 (60%) Dyspnoea: 23 (46%) Chills: 8 (16%) Chest pain: 5 (10%) Loss of taste or / and smell: 4 (8%) Sneeze: 2 (4%) Abdo symptoms: 1 (2%) Demographics: Median age 56 years (range 24–86) 32 (64%) male

Abdollahi 2020a (Continued)

Exposure history: Not stated

Index tests

Reference Sample: Nasopharyngeal (NP)

Sample collected by: Lab technician

Sample collection method: After collection of samples by patients, a nasopharyngeal sample (taken from the opposite nostril) was collected using a sterile Dacron swab with a plastic handle placed into a separate container with viral transport medium (VTM)

Sample storage/transport: Specimens were transported to a clinical laboratory within 30 minutes of collection and were processed soon after delivery.

Timing of sample collection: Not stated

NAAT extraction method: Viral Nucleic Acid Extraction kit (Cat. No. YVN50/YVN100) provided by RBC Bioscience, Taipei, Taiwan

Assay used: Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic Kit (PCR-Fluorescence Probing) of Sansure Biotech (S3102E) (Changsha, China) and a thermal cycler specified for CFX96™ Real-Time PCR Detection System (Bio-Rad Laboratories, Inc.)

Genetic target: Not stated

Threshold: Ct ≤ 35

Blinding reported: Yes

Threshold predefined: Yes

Index Sample: Nasopharyngeal (NP)

Sample collected by: Patient

Sample collection method: Before technician collected samples, written instructions provided for the patients. Specimens were obtained by a sterile Dacron swab with a plastic handle. Swab placed into a separate container with viral transport medium (VTM)

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Ct ≤ 35

Blinding reported: Yes

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Patient collected OP and NP samples immediately after each other.

Technician collected OP and NP samples immediately after each other.

All patients received all sampling methods: Yes

Abdollahi 2020a (Continued)

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: "No significant financial support for the work that could have influenced its outcome"

Publication status: published

Source: Iranian Journal of Pathology

Author COI: none stated by authors

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			

Abdollahi 2020a (Continued)

DOMAIN 2: Index test (Operator)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Abdollahi 2020b

Study characteristics

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Abdollahi 2020b (Continued)

Patient Sampling	Single-group study to estimate agreement between technician and self-collected nasopharyngeal and oropharyngeal samples for detection of Sars-CoV Design: 50 (28) adult patients with clinical and radiologic evidence of viral pneumonia admitted to an infectious diseases ward Recruitment: Random Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Inpatient Location: Imam Khomeini Hospital Complex, Tehran Country: Iran Dates: February 28 to April 27, 2020 Symptoms and severity: - Fever: 34 (68%) - Muscle pain: 30 (60%) - Cough: 30 (60%) - Dyspnoea: 23 (46%) - Chills: 8 (16%) - Chest pain: 5 (10%) - Loss of taste or / and smell: 4 (8%) - Sneeze: 2 (4%) - Abdo symptoms: 1 (2%) Demographics: Median age 56 years (range 24–86) 32 (64%) male Exposure history: Not stated
Index tests	Reference sample: oropharyngeal (OP) Sample collected by: lab technician Sample collection method: After collection of samples by patients, oropharyngeal samples were collected using a sterile Dacron swab with a plastic handle. Swab placed into a separate container with viral transport medium (VTM) Sample storage/transport: specimens were transported to a clinical laboratory within 30 minutes of collection and were processed soon after delivery. Timing of sample collection: Not stated NAAT extraction method: viral Nucleic Acid Extraction kit (Cat. No. YVN50/YVN100) provided by RBC Bioscience, Taipei, Taiwan Assay used: Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic Kit (PCR-Fluorescence Probing) of Sansure Biotech (S3102E) (Changsha, China) and a thermal cycler specified for CFX96™ Real-Time PCR Detection System (Bio-Rad Laboratories, Inc.) Genetic target: Not stated Threshold: Ct ≤ 35 Blinding reported: Yes Threshold predefined: Yes Index sample: oropharyngeal (OP)

Abdollahi 2020b (Continued)

Sample collected by: Patient

Sample collection method: Before technician collected samples, written instructions provided for the patients. Specimens were obtained by a sterile Dacron swab with a plastic handle and soon after collection, each swab was placed into a separate container with viral transport medium (VTM).

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Ct ≤ 35

Blinding reported: Yes

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Patient collected OP and NP samples immediately after each other.

Technician collected OP and NP samples immediately after each other.

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: 'No significant financial support for the work that could have influenced its outcome'.

Publication status: Published

Source: Iranian Journal of Pathology

Author COI: None stated by authors

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns
DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Yes

Was a case-control design avoided?

Yes

Did the study avoid inappropriate exclusions?

Unclear

Abdollahi 2020b (Continued)

Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	

Abdollahi 2020b (Continued)

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

AbdulRahman 2020a

Study characteristics

Patient Sampling Design: Unclear group of symptomatic individuals, staff, close contacts and preoperation patients tested in a COVID-19 clinic
Recruitment: Unclear
Prospective or retrospective: Unclear
Sample size (cases): 1009 (60)

Patient characteristics and setting Setting: Hospital outpatient
Location: Bahrain Defence Force Hospital
Country: Bahrain
Dates: October 2020
Symptoms and severity: Not stated
Demographics: Not stated
Exposure history: Not stated

Index tests **Reference sample:**
Nasopharyngeal swab
Sample collection device: Not stated
Sample collected by: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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AbdulRahman 2020a (Continued)

Sample collection method: The nasopharyngeal samples were transferred to a viral transport media immediately after collection and transported to a COVID-19 laboratory for testing; no more details provided

Sample storage/transport: VTM

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Thermo Fisher Scientific (Waltham, MA) Invitrogen on the Applied Biosystems (Foster City, CA) 7500 Fast Dx RealTime PCR Instrument

Genetic target: E, RdRP and N genes

Threshold: CT Values > 40 were considered negative.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample:

Saliva spit

Sample collection device: saliva collection tube, no details provided

Sample collected by: Unsupervised patient

Sample collection method: Patients were instructed not to drink, smoke or chew gum immediately beforehand. The patient will be instructed to spit into the tube. Saliva production can be helped by placing the tip of the tongue behind the front teeth.

Sample storage/transport: Dry/direct sampling. Saliva sample can be kept in the fridge for up to 72 hours.

Timing of sample collection: Not stated

NAT extraction method: As for reference index sample

Assay used: As for reference index sample

Genetic target: As for reference index sample

Threshold: As for reference index sample

Blinding reported: As for reference index sample

Threshold predefined: As for reference index sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding

Publication status: Pre-print

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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AbdulRahman 2020a (Continued)

Source: MedRxiv

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

AbdulRahman 2020a (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

AbdulRahman 2020b

Study characteristics

Patient Sampling	Design: Unclear group of symptomatic individuals, staff, close contacts and preoperation patients tested in a COVID-19 clinic Recruitment: Unclear Prospective or retrospective: Unclear Sample size (cases): 1009 (60)
Patient characteristics and setting	Setting: Hospital outpatient Location: Bahrain Defence Force Hospital Country: Bahrain Dates: October 2020 Symptoms and severity: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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AbdulRahman 2020b (Continued)

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample:

Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: The nasopharyngeal samples were transferred to a viral transport media immediately after collection and transported to a COVID-19 laboratory for testing; no more details provided

Sample storage/transport: VTM

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Thermo Fisher Scientific (Waltham, MA) Invitrogen on the Applied Biosystems (Foster City, CA) 7500 Fast Dx RealTime PCR Instrument

Genetic target: E, RdRP and N genes

Threshold: CT values > 40 were considered negative.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample:

Saliva spit

Sample collection device: saliva collection tube; no details provided

Sample collected by: Unsupervised patient

Sample collection method: Patients were instructed not to drink, smoke or chew gum immediately beforehand. The patient will be instructed to spit into the tube. Saliva production can be helped by placing the tip of the tongue behind the front teeth.

Sample storage/transport: Dry/direct sampling. Saliva sample can be kept in the fridge for up to 72 hours.

Timing of sample collection: Not stated

NAT extraction method: As for reference index sample

Assay used: As for reference index sample

Genetic target: As for reference index sample

Threshold: As for reference index sample

Blinding reported: As for reference index sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

AbdulRahman 2020b (Continued)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding

Publication status: Pre-print

Source: MedRxiv

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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AbdulRahman 2020b (Continued)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Aita 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and saliva sample types for diagnosis of SARS-CoV-2 Design: [1] 326 (0) 'screening' participants enrolled from the community [2] 43 confirmed COVID-19 patients with saliva samples available tested during hospitalisation (14-17 days) (not included in review) [3] subset of [2] with saliva samples available for measurement of IgA antibodies (not included in review) Recruitment: Unclear Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Community (screening) Location: University Hospital of Padova Country: Italy Dates: April 22 to April 30, 2020 Symptoms and severity: Not stated. Described as screening

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Aita 2020 (Continued)

	Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collection device: Not stated Sample collected by: Healthcare worker Sample collection method: Not stated Sample storage/transport: Not stated Timing of sample collection: Screening NAT extraction method: Not stated Assay used: RT-PCR; no details provided Genetic target: E gene Threshold: Not stated Blinding reported: Not stated Threshold predefined: Not stated Index Sample: Saliva Sample collection device: Salivette tubes (SARSTEDT Ag & Co, Numbrecht, Germany) Sample collected by: Patient Sample collection method: patients were asked to collect a saliva sample immediately before a nasopharyngeal swab. Saliva was collected using Salivette® tubes containing a cotton swab without preparation (SARSTEDT AG & Co, Numbrecht, Germany), patients being asked to remove the cotton swab from the Salivette® and chew it for about one minute to stimulate salivation. Finally, the patients had to return the swab with the absorbed saliva to the Salivette® and replace the stopper. Sample storage/transport: The Salivette® was stored at 4 °C immediately after collection and centrifuged at 4000 g for 5 min within 3 h from collection in order to ensure that saliva samples were clear. Timing of sample collection: Not stated Assay used: RT-PCR; no details provided Genetic target: E gene Threshold: Not stated Blinding reported: Not stated Threshold predefined: Not stated
Target condition and reference standard(s)	
Flow and timing	Sampling schedule prespecified: Not stated Time interval between sampling methods: "asked to collect a saliva sample immediately before a NP swab was taken for analysis"

Aita 2020 (Continued)

All patients received all sampling methods: No

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement

Publication status: Published paper

Source: Clinica Chimica Acta

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Unclear		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		

Aita 2020 (Continued)

Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Gargle)		
DOMAIN 2: Index test (Oral swab)		
DOMAIN 2: Index test (Oropharyngeal)		
DOMAIN 2: Index test (Collection method)		
DOMAIN 2: Index test (Oropharyngeal/nasal)		
DOMAIN 2: Index test (Nasal)		
DOMAIN 2: Index test (Oral rinse)		
DOMAIN 2: Index test (Operator)		
DOMAIN 3: Reference standard		
Could the reference standard, its conduct, or its interpretation have introduced bias?		
Are there concerns that the target condition as defined by the reference standard does not match the question?		
DOMAIN 4: Flow and timing		
Was there an appropriate interval between index tests?	Yes	
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Unclear	
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear	
Were results presented per patient?	Yes	
Were all patients included in the analysis?	Unclear	
Could the patient flow have introduced bias?		Unclear risk

Akgun Dogan 2021

Study characteristics

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Akgun Dogan 2021 (Continued)

Patient Sampling	Single-group study to estimate agreement between NP/OP, OP and saliva sample types Design: [1] 200 (98) consecutive symptomatic patients who met the possible case definition for COVID-19 and hospitalised with moderate-severe disease, and sampled within the first 24 hours after hospitalisation (day 0) [2] 59 symptomatic patients from group 1 re-tested on day 5 (not included in this review) Recruitment: [1] Consecutive meeting 'possible' COVID-19 case definition Prospective or retrospective: Prospective Additional inclusion criteria: history of fever or acute respiratory symptoms AND travel history from an endemic area of COVID-19 within 14 days OR history of contact with an individual who was confirmed or suspected of having COVID-19 OR hospitalisation because of respiratory tract infection Exclusion criteria: Patients admitted to ICU, not giving consent to study, incapable of providing saliva sample and patients under the age of 18
Patient characteristics and setting	Setting: Hospital inpatient Location: Umraniye Teaching and Research Hospital, Istanbul Country: Turkey Dates: Not stated Symptoms and severity: 120/200 860% with cough 110/200 (55%) with myalgia 80/200 (40%) with fever 89/200 (45%) with dyspnoea 13/200 (7%) with loss of smell & taste Demographics: Mean age: 54.9 ± 16.1 years Sex: 160/200 (53%) male Exposure history: Not stated
Index tests	Reference Sample: Naso/oropharyngeal (NP/OP) sample Sample collection device: Not stated Sample collected by: Assume HCW Sample collection method: Not stated Sample storage/transport: Not stated Timing of sample collection: On day 0 (within 24 hours of hospitalisation) NAT extraction method: IFU accessed and describes the RT-PCR kit as 'nucleic extraction and purification steps eliminated' Assay used: SARS-CoV-2 Direct Detection kit (Coyote Bioscience Co, Ltd.) Genetic target: ORF1ab, N genes Threshold: Both genes positive; CT value ≤ 29 Blinding reported: Not stated Threshold predefined: Yes

Akgun Dogan 2021 (Continued)

Index Sample [A] Oropharyngeal (OP)

Sample collection device: Falcon tube

Sample collected by:

A single trained HCW took all samples to avoid possible variation in collection technique.

Sample collection method: cotton swab into falcon tube containing VTM

Sample storage/transport: VTM; all samples were transferred to lab within 1 h of sampling and stored in the refrigerator.

Timing of sample collection: On day 0 (within 24 hours of hospitalisation)

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample [B]: Saliva

Sample collection device: Falcon tube

Sample collected by: Patient

Sample collection method: Saliva samples were collected before other samples. Participants were given brief explanations about the difference between saliva and sputum, then they were asked to give saliva samples prior to other samples by a drooling technique. They spit approximately 1 mL into the falcon tubes containing the viral transport medium.

Sample storage/transport: VTM; all samples were transferred to lab within 1 h of sampling and stored in the refrigerator.

Timing of sample collection: On day 0 (within 24 hours of hospitalisation)

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Simultaneously

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Akgun Dogan 2021 (Continued)

Indeterminate results: None reported

Comparative			
Notes	Funding: No funding received Publication status: Pre-print Source: MedRxiv Author COI: Authors declared no COI present.		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	

Akgun Dogan 2021 (Continued)

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? No

Could the conduct or interpretation of the index test have introduced bias?

High risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all in-

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Akgun Dogan 2021 (Continued)

dex tests (samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Al Suwaidi 2021
Study characteristics

Patient Sampling	Design: Single group of school children presenting for COVID-19 screening. Indications for testing included contact with confirmed COVID-19 patients, presence of presumptive symptoms or testing for return to school. Recruitment: Unclear (convenience sample) Prospective or retrospective: Prospective Sample size (cases): 476 (80) Additional inclusion criteria: 9 children had samples repeated; info available excluding these cases (extracted)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Dubai Health Authority (DHA) community-based screening centres Country: United Arab Emirates Dates: 1 to 23 October 2020 Symptoms and severity: 39/476 (8.1%) symptomatic Demographics: Age: Mean (SD): 10.8 (3.9) Sex: 277/476 (58.2%) male Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swab Sample collection device: Greiner Bio-One universal transport system (Greiner Bio-One, Kremsmünster, Austria). Sample collected by: Healthcare worker Sample collection method: NP swab specimens were obtained by trained healthcare personnel using standardised DHA NP swab collection protocol for COVID-19 screening Sample storage/transport: Both NP swab and saliva specimens were transported in cool boxes with ice packs to the DHA virology laboratory for processing (Universal Transport Medium).

Al Suwaidi 2021 (Continued)

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Allplex 2019-nCoV RT-PCR assay. EZ1 DSP Virus Kit (Qiagen, Hilden, Germany)

Genetic target:

N, E and RdRp genes

Blinding reported: Not stated

Threshold: A cycle threshold (Ct) of 40 was taken as the cut-off for a positive result for the target genes as per the manufacturer-provided protocol.

Threshold predefined: Not stated

Index sample: Saliva spit

Sample collection device: Sterile container

Sample collected by: Unsupervised patient

Sample collection method: Participants were asked to close their mouths, allow saliva to pool in the mouth for 1 or 2 minutes and then gently spit into the provided sterile container.

Sample storage/transport: Dry/direct sampling

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used:

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published paper

Source: Clinical Microbiology and Infection

Author COI: Authors declared no COI present.

Methodological quality

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Al Suwaidi 2021 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Al Suwaidi 2021 (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Unclear risk

Altawalah 2020

Study characteristics

Patient Sampling	Design: Single group of suspected COVID-19 patients admitted consecutively to the Al-Sabah, Jaber, and Alrazi Hospitals, Kuwait Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 891(362) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital inpatient Location: Al-Sabah, Jaber, and Alrazi Hospitals Country: Kuwait Dates: 19 to 21 July 2020 Symptoms and severity: Not stated

Altawalah 2020 (Continued)

	Demographics: Age: Not stated Sex: Not stated for whole sample. For NP +ve, 193/344 (56.1%) male Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swabs Sample collection device: A sterile tube Sample collected by: HCW Sample collection method: The swab was passed through the nostril until reaching the posterior nasopharynx and removed while rotating Sample storage/transport: VTM Timing of sample collection: Not stated NAT extraction method: MagMax Viral/Pathogen Nucleic Acid Isolation Kit (Thermo Fisher Scientific, Waltham, MA, USA) Assay usedTaqPath™ COVID-19 multiplex real-time RT-PCR test Genetic target: Orf1ab, N and S genes Threshold: cycle threshold (Ct) values < 37 for three SARS-CoV-2 targets Blinding reported: Not stated Threshold predefined: Yes Index Sample: Saliva deep throat Sample collection device: A sterile container, NOS Sample collected by: patient; no details provided Sample collection method: Whole saliva (≈1.5 mL) was collected after deep cough from the suspected patients into a sterile container. Sample storage/transport: VTM if viscous Timing of sample collection: Not stated NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: None reported Uninterpretable results: None reported Indeterminate results: 43 NP and 28 saliva samples equivocal. No 3 x 3 data provided

Altawalah 2020 (Continued)

Comparative

Notes

Funding: Ministry of Health, Kuwait

Publication status: Published paper

Source: Journal of Clinical Virology

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			

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Altawalah 2020 (Continued)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Unclear

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Amoo 2021

Study characteristics

Patient Sampling	Design: Asymptomatic and symptomatic individuals > 15 yrs presenting for testing at a drive-through COVID-19 centre Recruitment: Unclear: Individuals who gave verbal consent were enrolled. Prospective or retrospective: Prospective Sample size (cases): 216 (42) Additional inclusion criteria: One patient had previously tested COVID +ve.
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through

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Amoo 2021 (Continued)

Location: COVID-19 test centre located at the Nigerian Institute of Medical Research (NIMR), Lagos

Country: Nigeria

Dates: June-July, 2020

Symptoms and severity: 113/216 (52.3%) symptomatic

Demographics:

Age: Mean 35 (SD $\pm$ 14.2)

Sex: 122/216 (56.5%) male

Exposure history:

128/216 (59.3%) with known exposure to COVID-19 case

12/216 (5.6%) had contact with overseas travellers.

Index tests

Reference sample: NP swab (HCW)

Sample collection device: Not stated

Sample collected by: HCW Laboratory interpreted

Sample collection method: Collected after index sample. No further details

Sample storage/transport: Tested within 24 hours of collection (transport medium NOS)

Timing of sample collection: Not stated

NAT extraction method:

Assay used: Roche COBAS 6800 (Roche Molecular Systems, Rotkreuz, Switzerland)

Genetic target: ORF1ab

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample: NP swab (self-collected)

Sample collection device: As for reference sample

Sample collected by: Supervised patient
Laboratory interpreted

Sample collection method: Participants were asked to watch a video noting the procedure, after which they were given swabs and transport medium to collect their samples individually. Participants were monitored both on site by health professionals and remotely using 'Mobihealth consult'. This application allows health professionals to remotely monitor the sample collection process.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Amoo 2021 (Continued)

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Authors received no specific funding for this work.

Publication status: Published paper

Source: PLoS One

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

Amoo 2021 (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? No

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Unclear risk

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Babady 2021

Study characteristics

Patient Sampling

Design:

[1] Single group of MSKCC employees who completed an internally designed research electronic data capture screening tool designed to determine the need for COVID-19 testing, and have paired oral rinses and NP samples

[2] Single group of MSKCC employees who completed an internally designed research electronic data capture screening tool designed to determine the need for COVID-19 testing, and have paired saliva and NP samples

[3] Single group of MSKCC employees who completed an internally designed research electronic data capture screening tool designed to determine the need for COVID-19 testing, and have paired saliva and OP samples. Not extracted for this review (ineligible reference sample)

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): [1] 98 (35); [2] 87 (18)

Patient characteristics and setting

Setting: Other: HCW screening

Location: Memorial Sloan Kettering Cancer Center (MSKCC), New York

Country: USA

Dates: April 4 to May 11, 2020

Symptoms and severity: 224/285 (78.5%) symptomatic

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP swabs

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: NPS and OPS samples were collected using flocked swabs (CopanDiagnostics, Murrieta, CA) and placed in viral transport media.

Sample storage/transport: VTM. Stored at room temperature. Transported to the laboratory within the next 2 hours

Timing of sample collection: NS

NAT extraction method: NUCLISENS EasyMag (bioMérieux, Durham, NC)

Assay used: Laboratory developed real-time RT-PCR based on the CDC protocol

Genetic target: N1 and N2

Threshold: Samples were considered positive if both analytic targets N1 and N2 were detected.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (A): Oral rinse (sterile water)

Babady 2021 (Continued)

Sample collection device: sterile container; no details provided

Sample collected by: Unsupervised patient

Sample collection method: HCWs were asked to place 10 mL of sterile water in their mouth and, with mouth closed, swish for 15 seconds, without gargling and spit the water in a sterile container.

Sample storage/transport: Dry/direct sampling. Stored at room temperature; transported to the laboratory within the next 2 hours

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Index Sample (B):

Saliva deep throat

Sample collection device: sterile container; no details provided

Sample collected by: Unsupervised patient

Sample collection method: HCWs were first asked to swallow and then bring up saliva from the back of the throat and spit at least 3.0 mL of saliva into an empty sterile container.

Sample storage/transport: Dry/direct sampling. Stored at room temperature; transported to the laboratory within the next 2 hours

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear (just described as paired).

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

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Babady 2021 (Continued)

Notes

Funding: National Cancer Institute Cancer Center support

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			

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Babady 2021 (Continued)

DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

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Babady 2021 (Continued)

Were all patients included in the analysis?

Unclear

Could the patient flow have introduced bias?

Unclear risk

Banerjee 2021
Study characteristics

Patient Sampling

Design:

Single group of 335 children who had standard of care COVID-19 testing ordered by their health care provider

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): 110 (59)

Note this is an artificial prevalence based on matching cases and non-cases to achieve a prevalence of ~ 50%

Additional inclusion criteria: Saliva samples paired with the first 53 corresponding negative NPS (collected within the first 2 days of study initiation) and the first 57 corresponding positive NPS (collected over 3 weeks after study initiation) were tested by Aptima assay. One subject provided duplicate samples, 3 weeks apart, both of which were used for the study

Patient characteristics and setting

Setting: COVID-19 testing centre

Location: Childrens Mercy, Kansas City

Country: USA

Dates: Not stated

Symptoms and severity: 100/109 (91.7%) symptomatic

Demographics: Age: Mean (range): 10.8 years (5-14)

Sex: 55/110 (50.5%) males

Exposure history: 9/110 (8.1%) were asymptomatic with known COVID-19 exposure.

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: Respiratory specimen was also collected with a flocked, nylon nasopharyngeal (NP) swab (Jiangsu Hanheng Medical Technology Co., Ltd, China) during the same visit, by the nurse and placed in viral transport media (BD Universal Viral Transport Medium, BD Diagnostics, CA) for SOC testing

Sample storage/transport: BD Universal Viral Transport Medium, BD Diagnostics, CA. NS Samples were transported to the laboratory by same-day courier (within 8 hours of sample collection) and stored at 4 °C until testing was completed in the clinical laboratory within the next 2 days (except 4 specimens that were tested between 2 and 5 days from collection).

Timing of sample collection: NS

NAT extraction method: Not stated

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Banerjee 2021 (Continued)

Assay used: Aptima SARS-CoV-2 assay

Genetic target: ORF1ab gene threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample: Saliva drool

Sample collection device: 10 mL conical tube without any transport media

Sample collected by: Patient/parent

Sample collection method: Volunteer patients were given a saliva collection kit that included a 9.5" plastic white individually wrapped straw (U.S. Foods, Lenexa, KS) and 10 mL conical tube without any transport media) during their visit at the drive-through test centre and asked to fill their mouth with saliva and use the straw to fill the collection tube with 2 mL of saliva.

Sample storage/transport: Dry/direct and stored and transported as for reference sample

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published paper

Source: Journal of the Pediatric Infectious Disease Society

Author COI: Authors declared no COI present.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Banerjee 2021 (Continued)

Was a consecutive or random sample of patients enrolled?	No
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	High risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	No
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	

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Banerjee 2021 (Continued)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point No

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Becker 2020

Study characteristics

Patient Sampling	Single-group study to compare agreement of saliva & NPS samples for diagnosis of COVID-19 Design: [1] 'Diagnostic cohort' of outpatients 88 (17) symptomatic who met CDC criteria for clinical testing [2] Single 'Convalescent cohort' prior positive NPS. N = 24: 2/24 hospitalised at time of first testing. Not included in this review Recruitment: [1] Unclear. 'Patients undergoing simultaneous saliva and NPS between March 26-April 13 2020'. Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Community Location: University of Nevada and Renown Health (Reno, NV) Country: USA Dates: [1] March 26-April 13, 2020 Symptoms and severity: [1] Symptomatic meeting CDC criteria for clinical testing Demographics: Not stated Exposure history: Not stated

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Becker 2020 (Continued)

Index tests

Reference Sample: Nasopharyngeal (NP)

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: Swab. No further details

Sample storage/transport: Sent for testing at the Nevada State Public Health Testing Laboratory'. No further details

Timing of sample collection: Time of presentation for COVID-19 testing

NAT extraction method: Not stated

Assay used: CDC RT-qPCR assay

Genetic target: Not stated

Threshold: Positive for any gene target

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva

Sample collected by: Patient

Sample collection method: Sample collection device: Random allocation to the Oragene OGD-610 DNA collection kit (55/88) and Orasure OM-505 Microbiome collection kit (33/88)
No further details

Sample storage/transport: Proprietary nucleic acid stabilisation solution added by patient to saliva sample for both collection devices. Time delay ~24 hours (shipped overnight for testing at a high complexity CLIA laboratory. Samples were aliquoted upon receipt and immediately processed. Additional aliquots were stored at -20 C for subsequent processing).

Timing of sample collection: Time of presentation for COVID-19 testing

NAT extraction method: MagMax Viral/Pathogen RNA purification kit (ThermoFisher CAT: A42352)

Assay used: UCSD TaqPath Multiplex RT-PCR COVID-19 assay OR Helix Primerdesignv1

Genetic target: Taqpath: N; ORF 1ab; S
Primer: RdRp; PD-IEC

Threshold: Positive for any gene target

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Simultaneous
All patients received all sampling methods: No

Becker 2020 (Continued)

Missing data: [1] 17 saliva samples were not evaluated at one laboratory (UCSD) and a total of 6 NPS were not ordered by the attending physician (table 1)

Uninterpretable results: None reported

Indeterminate results: [1] 6 indeterminate UCSD TaqPath NP; 3 indeterminate UCSD TaqPath saliva; 2 indeterminate Helix Primerdesign v1 saliva

Comparative

Notes

Funding: No external funding was received.

Publication status: Pre-print

Source: medRxiv

Author COI: 6/11 authors employed by Helix (one of the laboratories)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	No		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		

Becker 2020 (Continued)

Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	No
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	High risk

Begum 2022

Study characteristics

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Begum 2022 (Continued)

Patient Sampling

Design: A cross-sectional study
Inclusion criteria were (i) all age groups; (ii) either sex; (iii) acute onset of fever or cough; OR (iv) acute onset of any three or more of the presented signs or symptoms, general weakness/fatigue, headache, myalgia, sore throat, runny nose, nasal congestion, dyspnoea, anorexia/nausea/vomiting, diarrhoea, and altered mental status.

Recruitment: Unclear
214 symptomatic participants who fulfilled WHO case definitions for COVID-19 and who had known rRT-PCR test results within the last 24 h, using NP swab

Prospective or retrospective: Retrospective

Sample size (cases): 214 (112)

Additional inclusion criteria: This is most likely a retrospective cross-sectional study which was conducted until a minimum number of D+ had been accrued.

Patient characteristics and setting

Setting: Unclear

Location: Virology Laboratory, Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Dhaka

Country: Bangladesh

Dates: May and August 2021

Symptoms and severity: 214/214 (100%) symptomatic

Demographics:

Age: Not stated

Sex: Not stated

Exposure history: Not stated

Index tests

Reference sample: NPS

Sample collection device: NS

Sample collected by: NS

Sample collection method: NS

Sample storage/transport: VTM

Timing of sample collection: 0 ≥ 7days pso

NAT extraction method: NS

Assay used: : Chemagic viral NA/gDNA kit (PerkinElmer, MA, USA) RT-PCR

Genetic target: ORF1ab (RdRp)

Threshold: Ct > 30)

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Nasal nos

Sample collection device: NS

Sample collected by: NS

Begum 2022 (Continued)

Sample collection method: NS

Sample storage/transport: VTM

Timing of sample collection: $0 \geq 7$ days pso

NAT extraction method: NS

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: In Tec PRODUCTS Inc. (one of the Ag tests evaluated) funded the study. Government of Bangladesh, Canada, Sweden, and the UK for providing core/un-restricted support

Publication status: Published paper

Source: Journal of Clinical Laboratory Analysis

Author COI: MR received funding from InTec PRODUCTS, INC., for this work. ZL and TK are scientific staff of InTec PRODUCTS, INC. but had no role in sample collection, laboratory evaluation, and analysis of this study. All other authors had no competing interests.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		

Begum 2022 (Continued)

Could the selection of patients have introduced bias?		Unclear risk
Are there concerns that the included patients and setting do not match the review question?		Unclear
DOMAIN 2: Index test (Saliva)		
DOMAIN 2: Index test (Gargle)		
DOMAIN 2: Index test (Oral swab)		
DOMAIN 2: Index test (Oropharyngeal)		
DOMAIN 2: Index test (Collection method)		
DOMAIN 2: Index test (Oropharyngeal/nasal)		
DOMAIN 2: Index test (Nasal)		
If a threshold was used, was it pre-specified?	Yes	
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear	
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes	
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear	
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Oral rinse)		
DOMAIN 2: Index test (Operator)		
DOMAIN 3: Reference standard		
Could the reference standard, its conduct, or its interpretation have introduced bias?		
Are there concerns that the target condition as defined by the reference standard does not match the question?		
DOMAIN 4: Flow and timing		

Begum 2022 (Continued)

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Benoit 2021

Study characteristics

Patient Sampling	Design: Single group of participants recruited from a dedicated COVID-19 screening clinic if they had symptoms of COVID-19 or if they had contact with a positive case Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 647 (134) Additional inclusion criteria: Total varies due to the number of invalid cases
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Two designated COVID-19 screening clinics in Quebec Country: Canada Dates: November and December 2020 Symptoms and severity: Not stated Quote: "Participants were recruited if they had symptoms of COVID-19 or if they had contact with a positive case". Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: Mixed NP/OP Sample collection device: Not stated Sample collected by: Healthcare worker (HCW) Sample collection method: ONPS was collected by a trained healthcare professional by swabbing the posterior oropharynx and then inserting the same swab through one nostril and rotating for 5–10 s before removing. Sample storage/transport: PCR media nos

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Benoit 2021 (Continued)

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: the Cobas® SARS-CoV-2 test on the cobas® 6800 in St-Eustache (n = 300) and the Cobas® 8800 in Montreal (n = 347) Genetic target: ORF1ab and E genes

Threshold: Samples were considered positive if they met the interpretation criteria of the manufacturer.

Blinding reported: Not stated threshold predefined: Yes

Index Sample: Spring water gargle

Sample collection device: Globet (ESKA®, St-Mathieu-d'Harricana)

Sample collected by: Unsupervised patient

Sample collection method: Collected after NP/OP swabs. Participants were asked not to eat, drink, or smoke for 15 min before. They were handed a goblet with 5 mL of natural spring water (ESKA®, St-Mathieu-d'Harricana) and were told to gargle with the water for 5 s in the mouth, 5 s in the throat, to repeat this process once and then to spit as much as possible in the initial goblet. They were then asked to transfer their gargle specimen into a tube that was sent to a designated laboratory for processing and testing.

Sample storage/transport: Natural spring water. Gargle specimens were split in the laboratory as follows: 1 mL was added to 4.3 mL of PCR media and 400 µL was added to 200 µL of Cobas® Omni Lysis Reagent for 10 min.

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: 3 participants with invalid results (excluded before processing) excluded for main analysis

Indeterminate results: None reported

Comparative

Notes

Funding: Ministère de la Santé du Québec; Roche Diagnostics

Publication status: Published paper

Source: Journal of Medical Virology

Author COI: No COI statement reported

Benoit 2021 (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	No		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			

Benoit 2021 (Continued)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)?

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Bhattacharya 2021

Study characteristics

Patient Sampling	Single-group study to compare agreement between NP and saliva sample types Design: 74 (58) suspected COVID-19 patients with mild-to-moderate symptoms from different COVID-19 care hospitals Recruitment: Not stated Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Unclear, probably hospital outpatients Location: Different COVID-19 care hospitals in Bhubaneswar Country: India Dates: Not stated

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Bhattacharya 2021 (Continued)

Symptoms and severity: All patients have 'mild to moderate' symptoms

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference Sample: Nasopharyngeal (NP)

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: Swab, no details provided

Sample storage/transport: Not stated

Timing of sample collection: Within 48 hours after symptoms onset

NAT extraction method: QIAamp Viral RNA Mini Kit (Qiagen)

Assay used: Cobas 6800 (Roche Molecular Diagnostics, Pleasanton, CA, USA)

Genetic target: ORF1, E genes

Threshold: Both genes positive or ORF1-positive

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample: Saliva

Sample collected by: Patient

Sample collection method: No details provided

Saliva specimens were collected by the patients themselves in sterile sputum containers.

Sample storage/transport: Not stated
'transported as per the standard guidelines'

Timing of sample collection: Within 48 hours after symptoms onset

NAT extraction method: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Not stated

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Not stated

Time interval between sampling methods: Not stated

All patients received all sampling methods: Not stated

Missing data: None reported

Uninterpretable results: None reported

Bhattacharya 2021 (Continued)

Indeterminate results: None reported

Comparative

Notes

Funding: ICMR

Publication status: Pre-print

Source: MedRxiv

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			

Bhattacharya 2021 (Continued)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Bidkar 2022

Study characteristics

Patient Sampling	Design: Single group of suspects aged 8 years and above presenting with a varied spectrum of illness of COVID-19
	Recruitment: Consecutive
	Prospective or retrospective: Prospective
	Sample size (cases): 80 (40)
	Additional inclusion criteria: None

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Bidkar 2022 (Continued)

Patient characteristics and setting	Setting: Hospital outpatient Location: One of the tertiary care teaching hospitals in central India, Nagpur city Country: India Dates: October-November 2020 Symptoms and severity: Not stated Demographics: Mean age: 36.4 y 49/80 (61.3%) males Exposure history: Not stated
Index tests	Reference sample: Mixed nasopharyngeal/oropharyngeal Sample collection device: Not stated Sample collected by: Healthcare worker Sample collection method: Conventional NP-OP swabs of suspects were collected by trained HCWs using Nylon swab sticks and transferred into viral transport medium (VTM) as per guidelines laid by statutory bodies. Sample storage/transport: VTM Timing of sample collection: Not stated NAT extraction method: SARSCoV-2 Nucleic Acid Diagnostic Kit, no details provided Assay Lab system RT-PCR kit Genetic target: ORF1ab and E genes Threshold: the cycle threshold (Ct) values of both target genes was ≤ 38. Blinding reported: Not stated Threshold predefined: Yes Index Sample: Saliva swab Sample collection device: Not stated Sample collected by: Supervised patient Sample collection method: The suspect was asked to give a gentle external massage to the submandibular gland region from outside for a period not less than 60 s. A broad-ended flocced Nylon swab stick was rolled in the floor of the oral cavity for 20–40 s by the suspect himself/herself. Sample storage/transport: VTM Timing of sample collection: Not stated NAT extraction method: As for the reference sample Assay used: As for the reference sample Genetic target: As for the reference sample Threshold: As for the reference sample

Bidkar 2022 (Continued)

Blinding reported: As for the reference sample

Threshold predefined: As for the reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: Inconclusive samples: 4 NP and 6 salivary samples

Comparative

Notes

Funding: Not funded

Publication status: Published paper

Source: Indian Journal of Otolaryngology and Head and Neck Surgery

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	No		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

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Bidkar 2022 (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Bikos 2021

Study characteristics

Patient Sampling	Design: Unclear group of individuals testing at the Montana State University (MSU) symptomatic testing site in Bozeman, MT, USA, between the days of mid-November 2020 Recruitment: Unclear (probably volunteers) Prospective or retrospective: Prospective Sample size (cases): 243 (70) Additional inclusion criteria: 1 result missing in Table 2 for SalivirDetect RT-PCR Information for SLAMP not relevant for this review; so not extracted
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Montana State University Country: USA Dates: mid-November 2020 Symptoms and severity: 170/243 (70%) symptomatic Demographics: Age: Median (range): 20 (17-63) Sex: 112/244 (45%) male Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swab Sample collection device: Not stated Sample collected by: Not stated Sample collection method: Not stated Sample storage/transport: Not stated Timing of sample collection: Not stated NAT extraction method: Plates were covered with sealing foil and heated to 95° C for 5 min in a standard thermocycler then cooled to 4° C. Assay used: Real-time PCR thermocycling was performed per CDC guidelines; no details provided Genetic target: N1, N2, and RNPS genes Threshold: Not stated Blinding reported: Not stated Threshold predefined: Not stated Index Sample: Saliva spit Sample collection device: SalivirDetect: 50 mL centrifuge tube Sample collected by: Unsupervised patient

Bikos 2021 (Continued)

Sample collection method: Approx. 5 mL of saliva was collected in a 50 mL centrifuge tube; no other details provided

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: The tube was placed in a 95 °C oven (Fisherbrand Isotemp General Purpose Heating and Drying Oven) for 45 min, then allowed to sit at room temperature to cool.

Assay used: NEB Luna Kit

Genetic target: N1 genes

Threshold: Not stated

Blinding reported: Threshold predefined: Not stated

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: State of Montana through the Coronavirus Aid, Relief and Economic Security Act (CARES) Act

Publication status: Pre-print

Source: MedRxiv

Author COI: Connie B. Chang and James N. Wilking are co-founders of ULTSafety, Inc. which has licenced technology from Montana State University and Harvard University relating to this publication.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		

Bikos 2021 (Continued)

Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Unclear
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	

Bikos 2021 (Continued)

Was there an appropriate interval between index tests?	Unclear
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Boerger 2021

Study characteristics

Patient Sampling	Design: Single group of adults, age 18 or older, who presented at an outpatient collection site for SARS-CoV-2 molecular testing Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 281 (35) Additional inclusion criteria: Authors provided information after retesting of discordant samples (not extracted as a priority) Insufficient information about the MT vs Saliva comparison (no info about indeterminate, no 2 x 2 table extracted)
Patient characteristics and setting	Setting: Hospital outpatient Location: Mayo Clinic, Rochester Country: USA Dates: Not stated Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal Sample collection device: Routine protocol, no details provided Sample collected by: Healthcare worker Sample collection method: Routine protocol, no details provided Sample storage/transport: Specimens were transported to the testing laboratory at 2 to 8 °C for SARS-CoV-2 PCR. The majority of specimens were tested

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Boerger 2021 (Continued)

within 3 days of collection. In the event that initial testing was delayed by 3 days post-collection, specimens were frozen at 280 °C for up to 2 weeks prior to testing.

Timing of sample collection: At contact with the COVID-19 centre

NAT extraction method: NucliSENS EMAG (bioMérieux; Durham, NC) or the Hamilton Microlab STAR (Hamilton; Reno, NV)

Assay used: Mayo Clinic laboratory-developed test

Blinding reported: Not stated

Genetic target: N gene

Threshold: Not stated

Threshold predefined: Not stated

Index Sample (A): Saliva spit

Sample collection device: OMNIgene-ORAL (OM-505) collection kit (DNA Genotek, Ottawa, Ontario, Canada)

Sample collected by: Unsupervised patient

Sample collection method: OMNIgene-ORAL (OM-505) collection kit (DNA Genotek, Ottawa, Ontario, Canada)

Sample storage/transport: OMNIgene-ORAL (OM-505) collection kit (DNA Genotek, Ottawa, Ontario, Canada)

Timing of sample collection: At contact with the COVID-19 centre

NAT extraction method: NucliSENS EMAG (bioMérieux; Durham, NC), the Hamilton Microlab STAR (Hamilton; Reno, NV) or the MagNA Pure 96 (Roche; Indianapolis, IN)

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Index Sample (B): Nasal mid-turbinate

Sample collection device: Not stated

Sample collected by: Unsupervised patient

Sample collection method: Patients used a flocked MT swab (Copan Diagnostics, Murrieta, CA) specimen from both nostrils.

Sample storage/transport: Not stated

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: NucliSENS EMAG (bioMérieux; Durham, NC) or the Hamilton Microlab STAR (Hamilton; Reno, NV)

Boerger 2021 (Continued)

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 51 samples not included in final paired analysis

Uninterpretable results: None reported

Indeterminate results: 1 (0.3%) NP swab and 4 (1.4%) saliva specimens yielded an indeterminate result.

Comparative

Notes

Funding: No funding disclosure

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Unclear		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		

Boerger 2021 (Continued)

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
If a threshold was used, was it pre-specified?	Unclear
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	

Boerger 2021 (Continued)

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? Unclear risk

Borghi 2021a

Study characteristics

Patient Sampling

Design: Single group of adults with paired samples attending the San Paolo Hospital in Milan

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): 192 (87)

Additional inclusion criteria: None

Patient characteristics and setting

Setting: Hospital, no further details provided

Location: San Paolo Hospital in Milan

Country: Italy

Dates: Not stated

Symptoms and severity: 80/192 (41.7%)

Demographics:
Age: Range 18-85 years
Sex: 91/192 (47.8%) males
Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Not stated

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Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: A qPCR using N1 (FAM, BHQ-1 labelled probe) and RP (Cy5, BHQ-1) primers/probes published by the Center for Disease Control and Applied Biosystem 7500 Fast instrument

Genetic target: N1 and RP primers

Threshold: Threshold predefined: Samples were considered positive upon detection of N1 (Ct < 40)

Blinding reported: Not stated threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Sterile 50 mL tube

Sample collected by: Patient/parent, no details provided

Sample collection method: A sterile dental cotton roll was kept for two minutes in the vestibular space next to the lower premolar-molar area, then under the tongue close to the Wharton duct opening for an additional two minutes.

Sample storage/transport: Dry/direct sampling. Once duly soaked with saliva, the dental roll was preserved in a sterile 50 mL tube, at room temperature until use (up to 7 days).

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published letter

Source: Pharmacological Research

Borghi 2021a (Continued)

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

Borghi 2021a (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Borghi 2021b

Study characteristics

Patient Sampling	Design: Single group of adults with paired samples attending the San Paolo Hospital in Milan Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 192 (87) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital, no further details provided Location: San Paolo Hospital in Milan Country: Italy Dates: Not stated Symptoms and severity: 80/192 (41.7%)

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Borghi 2021b (Continued)

Demographics:
Age:
Range 18-85 years
Sex: 91/192 (47.8%) males

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: A qPCR using N1 (FAM, BHQ-1 labelled probe) and RP (Cy5, BHQ-1) primers/probes published by the Center for Disease Control and Applied Biosystem 7500 Fast instrument

Genetic target: N1 and RP primers

Threshold: Threshold predefined: Samples were considered positive upon detection of N1 (Ct < 40)

Blinding reported: Not stated threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Sterile 50 mL tube

Sample collected by: Patient/parent, no details provided

Sample collection method: A sterile dental cotton roll was kept for two minutes in the vestibular space next to the lower premolar-molar area, then under the tongue close to the Wharton duct opening for an additional two minutes.

Sample storage/transport: Dry/direct sampling. Once duly soaked with saliva, the dental roll was preserved in a sterile 50 mL tube, at room temperature until use (up to 7 days).

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Borghi 2021b (Continued)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published letter

Source: Pharmacological Research

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			

Borghi 2021b (Continued)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Borghi 2021c

Study characteristics

Patient Sampling	Design: Single group of children with paired samples attending at Vittore Buzzi Children's Hospital Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 109 (27) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital; no further details provided Location: Vittore Buzzi Children's Hospital Country: Italy Dates: Not stated Symptoms and severity: [a] 80/192 (41.7%)

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Borghi 2021c (Continued)

[b] Not stated

Demographics:

Age: Range 0-17 years

Sex: 58/109 (53.6%) males

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: A qPCR using N1 (FAM, BHQ-1 labelled probe) and RP (Cy5, BHQ-1) primers/probes published by the Center for Disease Control and Applied Biosystem 7500 Fast instrument

Genetic target: N1 and RP primers

Threshold: Samples were considered positive upon detection of N1 (Ct < 40)

Blinding reported: Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Sterile 50 mL tube

Sample collected by: Patient/parent; no details provided

Sample collection method: A sterile dental cotton roll was kept for two minutes in the vestibular space next to the lower premolar-molar area, then under the tongue close to the Wharton duct opening for an additional two minutes.

Sample storage/transport: Dry/direct sampling. Once duly soaked with saliva the dental roll was preserved in a sterile 50 mL tube, at room temperature until use (up to 7 days).

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

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Borghi 2021c (Continued)

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published letter

Source: Pharmacological Research

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Borghi 2021c (Continued)

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Boutros 2021(a)

Study characteristics

Patient Sampling	Design: Adults referred by their attending physician because of recent symptoms of COVID-19 Recruitment: Consecutive Prospective or retrospective: Prospective

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Boutros 2021(a) (Continued)

Sample size (cases): 147 (59)
Additional inclusion criteria: Some patients declined to participate in the study (n = 11) and others declined to perform NP once OS had been performed (n = 2).

Patient characteristics and setting

Setting: COVID-19 testing centre/drive-through

Location: Nice-Côte d'Azur Metropolis free COVID-19 screening centre, Nice

Country: France

Dates: 21 September 2020-6 January 2021

Symptoms and severity: 147/147 (100%)

Demographics:

Mean age 40 (SD 15)

Sex: 61/147 (41.4%) male

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Nylon swabs type A-04; Jiangsu Han-Heng Medical Technology Co., Ltd., Changzhou, China

Sample collected by: Not stated

Sample collection method:

Swabs were eluted into a vial containing viral transport medium.

ONS and NPS sampled in random order

Sample storage/transport: Viral Transport Medium (VTM). Samples were received within 4 h at the laboratory.

Timing of sample collection: Most participants (107/147, 72.8%) were sampled within 4 days of symptom onset. The interval between symptom onset and testing was 3.6 ± 2.6 days.

NAT extraction method: Not stated

Assay used: RT-PCR, Da An Gene DA0992-Detection Kit for 2019-nCoV (Da An Gene Co., Ltd., Sun Yat-sen University, Guangzhou, China) Idylla SARS-CoV-2 test cartridges (reference A1043/6; Biocartis, Mechelen, Belgium)

Genetic target: N, Orf1b genes threshold: N and/or Orf1b genes # 36

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Small hydroxylated polyvinyl acetate (PVA) sponges; Merocel® Standard Dressing, réf 400400; Medtronic, Dublin, Ireland

Sample collected by: Supervised patient ('All 409 participants performed the saliva self-sampling with the OS correctly as explained.')

Sample collection method: Sponges were placed in the mouth for 1 minute and inserted into a sterile collection tube by the subjects themselves. No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette.

ONS and NPS sampled in random order.

Sample storage/transport: Dry/direct sampling

Timing of sample collection: As for reference sample

Boutros 2021(a) (Continued)

NAT extraction method: No RNA extraction

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Some patients declined to perform NP once OS had been performed (n = 2).

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by Conseil Départemental 06, Ville de Nice, Métropole Nice Côte d'Azur, Fonds de Dotation AVENI and private donors

Publication status: Published paper

Source: ERJ Open Research

Author COI: P. Hofman is a member of the scientific advisory board (group of European experts) of Biocartis; however, this board is totally independent of Biocartis.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Boutros 2021(a) (Continued)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes

Boutros 2021(a) (Continued)

Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Boutros 2021 (b)

Study characteristics

Patient Sampling	Design: Adults referred by the contact tracing staff of the French public health insurance, considered as close contacts of a laboratory-confirmed COVID-19 case Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 262 (57) Additional inclusion criteria: Some patients declined to participate in the study (n = 11) and others declined to perform NP once OS had been performed (n = 2).
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Nice-Côte d'Azur Metropolis free COVID-19 screening centre, Nice Country: France Dates: 6 February-8 March, 2021 Symptoms and severity: 0/262 (0%) Demographics: Mean age 41 (SD 15) Sex: 117/262 (44.6%) male Exposure history: [b] 262/262 (100%) with known exposure to COVID case
Index tests	Reference sample: NP swab Sample collection device: Nylon swabs type A-04; Jiangsu Han-Heng Medical Technology Co., Ltd., Changzhou, China Sample collected by: Not stated Sample collection method: Swabs were eluted into a vial containing viral transport medium. ONS and NPS sampled in random order Sample storage/transport: Viral Transport Medium (VTM) Samples were received within 4 h at the laboratory. Timing of sample collection: Most participants (107/147, 72.8%) were sampled within 4 days of symptom onset. The interval between symptom onset and testing was 3.6 ± 2.6 days.

Boutros 2021 (b) (Continued)

NAT extraction method: Not stated

Assay used: RT-PCR, Da An Gene DA0992-Detection Kit for 2019-nCoV (Da An Gene Co., Ltd., Sun Yat-sen University, Guangzhou, China) Idylla SARS-CoV-2 test cartridges (reference A1043/6; Biocartis, Mechelen, Belgium)

Genetic target: N, Orf1b genes threshold: N and/or Orf1b genes # 36

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Small hydroxylated polyvinyl acetate (PVA) sponges; Merocel® Standard Dressing, réf 400400; Medtronic, Dublin, Ireland

Sample collected by: Supervised patient ('All 409 participants performed the salivary self-sampling with the OS correctly as explained.')

Sample collection method: Sponges were placed in the mouth for 1 minute and inserted into a sterile collection tube by the subjects themselves. No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette.

ONS and NPS sampled in random order

Sample storage/transport: Dry/direct sampling

Timing of sample collection: As for reference sample

NAT extraction method: No RNA extraction

Assay used: TMA no further details

Genetic target:

Threshold: NS

Blinding reported: NS

Threshold predefined: NS

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Some patients declined to perform NP once OS had been performed (n = 2).

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by Conseil Départemental 06, Ville de Nice, Métropole Nice Côte d'Azur, Fonds de Dotation AVENI and private donors

Publication status: Published paper

Source: ERJ Open Research

Author COI: P. Hofman is a member of the scientific advisory board (group of European experts) of Biocartis; however, this board is totally independent of Biocartis.

Boutros 2021 (b) (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			

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Boutros 2021 (b) (Continued)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Low risk

Bruxvoort 2021

Study characteristics

Patient Sampling	Design: Single group of adult patients presenting to EDs with acute symptoms and concern about COVID-19 were eligible to participate in the study if their attending physician placed an order for a standard NP/OP SARS-CoV-2 test. Recruitment: Only patients with all three specimens collected were included in the main analysis. Prospective or retrospective: Prospective Sample size (cases): 2112 (335) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Emergency Department Location: 7 EDs at Kaiser Permanente Southern California (KPSC)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Bruxvoort 2021 (Continued)

Country: USA

Dates: 18 August to 2 November 2020

Symptoms and severity: All participants symptomatic at testing time

Demographics: Age:

864/2112 (40.9%) 18-39 years

647/2112 (30.6%) 40-59 years

601/2112 (28.5%) ≥ 60 years

Sex: 952/2112 (45.1%) male

Exposure history: Not stated

Index tests

Reference sample: Mixed NP/OP

Sample collection device: A tube with VTM; no details provided

Sample collected by: Healthcare worker

Sample collection method: NP/OP specimens were collected by nurses using a long, thin swab to swab the back of the throat, avoiding the tongue, followed by inserting the same swab into one nostril parallel to the palate for a few seconds to absorb nasopharyngeal secretions.

Sample storage/transport: VTM 26 hours approximately

Timing of sample collection: 0 ≥ 7 days after symptoms onset

NAT extraction method: Not stated

Assay used: Roche cobas® SARS-CoV-2 assay on the Roche cobas® 8800 System

Genetic target: ORF1ab and E genes

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample (A): Saliva

Sample collection device: SpectrumDNA™ saliva collection device (Spectrum Solutions, Draper, UT)

Sample collected by: Supervised patient

Sample collection method: Per manufacturer instructions, patients were asked to 1) provide approximately 2 mL of spit into the collection tube measured by a standardised wavy black line, 2) screw on a separate cap to release a stabilising solution, and 3) shake for 5 s.

Sample storage/transport: dry/direct sampling. No further details.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Bruxvoort 2021 (Continued)

Threshold predefined: Not stated

Index Sample (B): Nasal anterior nares

Sample collection device: A tube with VTM; no details provided

Sample collected by: Supervised patient

Sample collection method: Anterior nares swabs were collected by asking the patient to insert a shorter, thicker swab less than 1 in. into the nostril, rotate the swab against the nostril wall several times, repeat with the other nostril.

Sample storage/transport: VTM

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: Not stated

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 81 pairs excluded due to one of the samples being missing.

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: the Regional Research Committee of Kaiser Permanente Southern California and Kaiser Permanente Southern California Internal Research Funds

Publication status: Published paper

Source: American Journal of Emergency Medicine

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		

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Bruxvoort 2021 (Continued)

Was the intention that patients receive all tests at all time points? No

Could the selection of patients have introduced bias? High risk

Are there concerns that the included patients and setting do not match the review question? Unclear

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? No

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? High risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? No

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Bruxvoort 2021 (Continued)

Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk

Callahan 2021(a)

Study characteristics

Patient Sampling	Design: [1] Single group of subjects presenting for their first COVID-19 test 'clinically suspected of COVID-19' [2] Single group of subjects with a previous positive test presenting for follow-up [preselected population, not extracted] Recruitment: Unclear Prospective or retrospective: Unclear Sample size (cases): [1] Initial (general): 196 (35) This was calculated by adding up TP, FN and FP for shallow and deep nasal samples combined in the initial tested group.

Callahan 2021(a) (Continued)

Additional inclusion criteria: Participants are assigned to different procedures and transport method arm; initial (no prior test) for deep (mid-turbinate) separate to shallow (ant nares) further subdivided into dry swab separate to use of any transport medium (VTM or GITC) extracted for this review

Patient characteristics and setting

Setting: Unclear

Location: Beth Israel Deaconess Medical Center (BIDMC) drive-through/walk-up ("drive-through") COVID-19 testing sites

Country: USA

Dates: Not stated

Symptoms and severity: Not stated 'Clinically suspected of COVID-19'

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The NP swab used was the Copan BD ESwab collection and transport system swab, with a head of flocked nylon (catalog no. 220532; Copan Diagnostics, Inc., Murietta, CA). 'Standard swab procedure'

Sample storage/transport: 3 mL VTM. 4 to 14 h for each pair of NP/nasal swabs from the same subject

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Abbott RealTime SARS-CoV-2 assay for EUA

Genetic target: RdRp and N genes

Threshold: Positivity: above the reporting threshold of 31.5

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (B): Nasal-mid-turbinate (deep method)

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The nasal swab used was the included Abbot swab for the GITC arm and the Hologic Aptima multitest swab otherwise (catalog no. AW-14334-001-003; Hologic, Inc., Marlborough, MA), all with polyester/nylon/rayon spun material. The swab was inserted into the naris until resistance was felt, and the swab was then rotated for 15 seconds without external pressure (Fig. S1b); this procedure was repeated with the same swab on the other naris

Sample storage/transport: Modified CDC viral transport medium (VTM) (Hanks' balanced salt solution containing 2% heat-inactivated foetal bovine serum [FBS], or GITC or DRY

4 to 14 h for each pair of NP/nasal swabs from the same subject

Callahan 2021(a) (Continued)

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Not stated

Genetic target: As for the reference sample

Threshold: As for the reference sample

Blinding reported: As for the reference sample

Threshold predefined: As for the reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: The Harvard Clinical and Translational Science Center (National Center for Advancing Translational Sciences, National Institutes of Health Award U

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	

Callahan 2021(a) *(Continued)*

Are there concerns that the included patients and setting do not match the review question?

Unclear

DOMAIN 2: Index test (Saliva)

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

Callahan 2021(a) (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Unclear
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Callahan 2021(b)

Study characteristics

Patient Sampling	Design: [1] Single group of subjects presenting for their first COVID-19 test 'clinically suspected of COVID-19' [2] single group of subjects with a previous positive test presenting for follow-up [pres-elected population, not extracted] Recruitment: Unclear Prospective or retrospective: Unclear Sample size (cases): [1] Initial (general): 196 (35) This was calculated by adding up TP, FN and FP for shallow and deep nasal samples combined in the initial tested group. Additional inclusion criteria: Participants were assigned to different procedures and transport method arm; initial (no prior test) for deep (mid-turbinate) separate to shallow (ant nares) further subdivided into dry swab separate to any transport medium (VTM or GITC) extracted for this review
Patient characteristics and setting	Setting: Unclear Location: Beth Israel Deaconess Medical Center (BIDMC) drive-through/walk-up ("drive-through") COVID-19 testing sites Country: USA Dates: Not stated Symptoms and severity: Not stated 'Clinically suspected of COVID-19' Demographics: Not stated

Callahan 2021(b) (Continued)

Exposure history: Not stated

Index tests

Reference sample: NP

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The NP swab used was the Copan BD ESwab collection and transport system swab, with a head of flocked nylon (catalog no. 220532; Copan Diagnostics, Inc., Murietta, CA). 'Standard swab procedure'

Sample storage/transport: 3 mL VTM. 4 to 14 h for each pair of NP/nasal swabs from the same subject

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Abbott RealTime SARS-CoV-2 assay for EUA

Genetic target: RdRp and N genes

Threshold: Positivity: above the reporting threshold of 31.5

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (B): Nasal-mid-turbinate (deep method)

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The nasal swab used was the included Abbot swab for the GITC arm and the Hologic Aptima multitest swab otherwise (catalog no. AW-14334-001-003; Hologic, Inc., Marlborough, MA), all with polyester/nylon/rayon spun material. The swab was inserted into the naris until resistance was felt, and the swab was then rotated for 15 seconds without external pressure (Fig. S1b); this procedure was repeated with the same swab on the other naris.

Sample storage/transport: Modified CDC viral transport medium (VTM) (Hanks' balanced salt solution containing 2% heat-inactivated foetal bovine serum [FBS], or GITC or DRY

4 to 14 h for each pair of NP/nasal swabs from the same subject

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Not stated

Genetic target: As for the reference sample

Threshold: As for the reference sample

Blinding reported: As for the reference sample

Threshold predefined: As for the reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Callahan 2021(b) *(Continued)*

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: The Harvard Clinical and Translational Science Center (National Center for Advancing Translational Sciences, National Institutes of Health Award U

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Callahan 2021(b) *(Continued)*

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	No

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Callahan 2021(b) *(Continued)*

Could the patient flow have introduced bias?

High risk

Callahan 2021(c)
Study characteristics
Patient Sampling

Design: [1] Single group of subjects presenting for their first COVID-19 test 'clinically suspected of COVID-19'
[2] single group of subjects with a previous positive test presenting for follow-up [preselected population, not extracted]

Recruitment: Unclear

Prospective or retrospective: Unclear

Sample size (cases): [1] Initial (general): 196 (35)
This was calculated by adding up TP, FN and FP for shallow and deep nasal samples combined in the initial tested group.

Additional inclusion criteria: Participants were assigned to different procedures and transport method arm; initial (no prior test) for deep (mid-turbinate) separate to shallow (ant nares) further subdivided into dry swab separate to any transport medium (VTM or GTC) extracted for this review

Patient characteristics and setting

Setting: Unclear

Location: Beth Israel Deaconess Medical Center (BIDMC) drive-through/walk-up ("drive-through") COVID-19 testing sites

Country: USA

Dates: Not stated

Symptoms and severity: Not stated 'Clinically suspected of COVID-19'

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The NP swab used was the Copan BD ESwab collection and transport system swab, with a head of flocked nylon (catalog no. 220532; Copan Diagnostics, Inc., Murietta, CA). 'Standard swab procedure'

Sample storage/transport: 3 mL VTM. 4 to 14 h for each pair of NP/nasal swabs from the same subject

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Abbott RealTime SARS-CoV-2 assay for EUA

Genetic target: RdRp and N genes

Callahan 2021(c) (Continued)

Threshold: Positivity: above the reporting threshold of 31.5

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (A): Nasal anterior nares (- shallow method)

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The nasal swab used was the included Abbot swab for the GITC arm and the Hologic Aptima multitest swab otherwise (catalog no. AW-14334-001-003; Hologic, Inc., Marlborough, MA), all with polyester/nylon/rayon spun material. The swab tip was inserted into the nostril, the patient was told to press a finger against the exterior of that naris, and the swab was rotated against this external pressure for 10 seconds; this procedure was repeated with the same swab on the other naris.

Sample storage/transport: Modified CDC viral transport medium (VTM) (Hanks' balanced salt solution containing 2% heat-inactivated foetal bovine serum [FBS], or GITC or DRY

4 to 14 h for each pair of NP/nasal swabs from the same subject

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: As for the reference sample

Genetic target: As for the reference sample

Threshold: As for the reference sample

Blinding reported: As for the reference sample

Threshold predefined: As for the reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: The Harvard Clinical and Translational Science Center (National Center for Advancing Translational Sciences, National Institutes of Health Award U

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

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Callahan 2021(c) (Continued)

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear

DOMAIN 2: Index test (Saliva)

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk

Callahan 2021(c) *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias?

Unclear risk

Callahan 2021(d)
Study characteristics

Patient Sampling	Design: [1] Single group of subjects presenting for their first COVID-19 test 'clinically suspected of COVID-19' [2] single group of subjects with a previous positive test presenting for follow-up [preselected population, not extracted] Recruitment: Unclear Prospective or retrospective: Unclear Sample size (cases): [1] Initial (general): 196 (35) This was calculated by adding up TP, FN and FP for shallow and deep nasal samples combined in the initial tested group.

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Callahan 2021(d) (Continued)

Additional inclusion criteria: Participants were assigned to different procedures and transport method arm; initial (no prior test) for deep (mid-turbinate) separate to shallow (ant nares) further subdivided into dry swab separate to any transport medium (VTM or GITC) extracted for this review

Patient characteristics and setting

Setting: Unclear

Location: Beth Israel Deaconess Medical Center (BIDMC) drive-through/walk-up ("drive-through") COVID-19 testing sites

Country: USA

Dates: Not stated

Symptoms and severity: Not stated 'Clinically suspected of COVID-19'

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The NP swab used was the Copan BD ESwab collection and transport system swab, with a head of flocked nylon (catalog no. 220532; Copan Diagnostics, Inc., Murietta, CA). 'Standard swab procedure'

Sample storage/transport: 3 mL VTM. 4 to 14 h for each pair of NP/nasal swabs from the same subject

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Abbott RealTime SARS-CoV-2 assay for EUA

Genetic target: RdRp and N genes

Threshold: Positivity: above the reporting threshold of 31.5

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (A): Nasal anterior nares (- shallow method)

Sample collection device: Collection tube

Sample collected by: Healthcare worker

Sample collection method: The nasal swab used was the included Abbot swab for the GITC arm and the Hologic Aptima multitest swab otherwise (catalog no. AW-14334-001-003; Hologic, Inc., Marlborough, MA), all with polyester/nylon/rayon spun material. The swab tip was inserted into the nostril, the patient was told to press a finger against the exterior of that naris, and the swab was rotated against this external pressure for 10 seconds; this procedure was repeated with the same swab on the other naris.

Sample storage/transport: Modified CDC viral transport medium (VTM) (Hanks' balanced salt solution containing 2% heat-inactivated foetal bovine serum [FBS], or GITC or DRY

4 to 14 h for each pair of NP/nasal swabs from the same subject

Callahan 2021(d) *(Continued)*

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: As for the reference sample

Genetic target: As for the reference sample

Threshold: As for the reference sample

Blinding reported: As for the reference sample

Threshold predefined: As for the reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: The Harvard Clinical and Translational Science Center (National Center for Advancing Translational Sciences, National Institutes of Health Award U

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	

Callahan 2021(d) (Continued)

Are there concerns that the included patients and setting do not match the review question?

Unclear

DOMAIN 2: Index test (Saliva)

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

Callahan 2021(d) (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Unclear
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Callahan 2021(e)

Study characteristics

Patient Sampling	Design: Unclear group of adults presenting for either initial or follow-up testing for COVID-19. Only initial testing group extracted for this review. Participants included a mix of symptomatic and asymptomatic patients. Recruitment: Convenience. 'After several days of collection, resulting in a majority of negatives, only (NP) positives were included to minimise clinical burden on laboratory staff'. Prospective or retrospective: Prospective Sample size (cases): Initial assessment: 343 (68) Additional inclusion criteria: Separate data by treated/untreated saliva samples and by PCR assay not available (mixed with follow-up samples)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: BIDMC and Beth Israel Deaconess Chelsea, Boston Country: USA Dates: Not stated Symptoms and severity: Mix of symptomatic and asymptomatic; no details provided Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swab

Callahan 2021(e) (Continued)

Sample collection device: A vial containing viral transport medium; no other details provided

Sample collected by: Healthcare worker

Sample collection method: NP swab was inserted into the nasopharynx and rotated for 10 s.

Sample storage/transport: VTM

Timing of sample collection: Saliva specimens were individually bagged and transported together with the NP specimen via courier to BIDMC's central laboratory for testing. Specimens were transported at room temperature.

NAT extraction method: Not stated

Assay used: Abbott m2000 RealTime SARS-CoV-2 assay on an Abbott m2000 RealTime system ("m2000") or the Abbott Alinity m system ("Alinity")

Genetic target: Not stated

Threshold: Cut-off for positive was a Ct value of 31.5 on the m2000 and 42 on the Alinity m.

Blinding reported: Not stated

Threshold predefined: Yes

Index sample: Saliva spit

Sample collection device: Sterile sample collection cup (VWR International; part no. 76299-868)

Sample collected by: Unsupervised patient

Sample collection method: While waiting in line for NP testing, each participant was given a sterile sample collection cup (VWR International; part no. 76299-868) and asked to spit/drool into a clearly labelled 3 mL fill line. No exclusions were made on the basis of recent consumption of food or drink or of smoking, and participants were not asked to rinse the mouth or perform any other preparation ahead of sample collection. They were informed that 3 mL is a large amount of saliva and may take several minutes/deposits to achieve and that thinking of a favourite food may help trigger salivation.

Sample storage/transport: Dry/direct sampling

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Callahan 2021(e) (Continued)

Uninterpretable results: None reported

Indeterminate results: Leaking samples and internal-control failures were omitted from analysis.

Comparative

Notes

Funding: Abbott Molecular

Publication status: Published paper

Source: Microbiology Spectrum

Author COI: C. Callahan, S. Ditelberg, S. Dutta, N. Littlehale, A. Cheng, K. Kupczewski, D. McVay, S. Riedel, and R. Arnaout have no other potential conflicts of interest to declare. J.E. Kirby has received reagents from Abbott Molecular for unrelated studies under a COVID-19 diagnostics evaluation agreement.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

Callahan 2021(e) *(Continued)*

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes

Callahan 2021(e) (Continued)

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias?

High risk

Castelain 2021

Study characteristics

Patient Sampling	Design: Single group of 501 individuals from residential care homes for the elderly (193 residents, 308 caregivers and administrative staff) participated in screening for SARS-CoV-2. Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 501 (26) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Other (residential care homes) Location: Amiens Picardie University Hospital Country: France Dates: May 6 to 13, 2020 Symptoms and severity: 104/501 (20.7%) symptomatic Demographics: Age mean (SD): 56.3 ± 22.2 102/501 (20.4%) males Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swab Sample collection device: Not stated Sample collected by: Healthcare worker Sample collection method: Not stated Sample storage/transport: VTM Timing of sample collection: Not stated NAT extraction method: Automated sample preparation using magnetic microparticles (Abbott mSample Preparation System DNA) Assay used: Abbott RealTime SARS-CoV-2 assay Genetic target: RdRp and N genes Threshold: Not stated Blinding reported: Not stated Threshold predefined: Not stated Index Sample: Saliva swab

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Castelain 2021 (Continued)

Sample collection device: Not stated

Sample collected by: Healthcare worker

Sample collection method: The saliva sample was collected by swabbing the fluid in the groove at the base of the lower jaw.

Sample storage/transport: VTM

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Not stated

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: Not stated

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: The University Hospital Center of Amiens and the University of Picardie - Jules Verne

Publication status: Published paper

Source: New Microbiologica

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear

Castelain 2021 (Continued)

Could the selection of patients have introduced bias?		Unclear risk
Are there concerns that the included patients and setting do not match the review question?		Unclear
DOMAIN 2: Index test (Saliva)		
If a threshold was used, was it pre-specified?	Yes	
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear	
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes	
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear	
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Low concern
DOMAIN 2: Index test (Gargle)		
DOMAIN 2: Index test (Oral swab)		
DOMAIN 2: Index test (Oropharyngeal)		
DOMAIN 2: Index test (Collection method)		
DOMAIN 2: Index test (Oropharyngeal/nasal)		
DOMAIN 2: Index test (Nasal)		
DOMAIN 2: Index test (Oral rinse)		
DOMAIN 2: Index test (Operator)		
DOMAIN 3: Reference standard		
Could the reference standard, its conduct, or its interpretation have introduced bias?		
Are there concerns that the target condition as defined by the reference standard does not match the question?		
DOMAIN 4: Flow and timing		
Was there an appropriate interval between index tests?	Unclear	
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all	Yes	

Castelain 2021 (Continued)

patients receive all index tests (samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Chu 2021 (a)
Study characteristics

Patient Sampling	Design: Single group of eligible ambulatory participants who presented to Groote Schuur Hospital in Cape Town, South Africa, for SARS-CoV-2 testing, before replacement of wild-type virus with the beta VoC Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 300 (33) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital outpatient Location: The Groote Schuur Hospital, Cape Town Country: South Africa Dates: August 1, 2020 to January 16, 2021 Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW Sample collection method: Not stated Sample storage/transport: Not stated Timing of sample collection: Not stated NAT extraction method: Not stated Assay used: RT-PCR Genetic target: targeting the S gene; no further details provided Threshold: Not stated

Chu 2021 (a) (Continued)

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Index Sample (B): Nasal mid-turbinate

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: the Wellcome Trust

Chu 2021 (a) (Continued)

Publication status: Published correspondence

Source: Lancet Infectious Diseases

Author COI: CM, HC, CW, DH, and AB report grants from the Wellcome Trust during the conduct of the study. CYC declares no competing interests.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Unclear		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			

Chu 2021 (a) (Continued)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Unclear

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Chu 2021 (b)

Study characteristics

Patient Sampling

Design: Single group of eligible ambulatory participants who presented to Groote Schuur Hospital in Cape Town, South Africa, for SARS-CoV-2 testing, after replacement of wild-type virus with the beta VoC

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): 107 (40)

Additional inclusion criteria: None

Patient characteristics and setting

Setting: Hospital outpatient

Location: The Groote Schuur Hospital, Cape Town

Country: South Africa

Dates: August 1, 2020 to January 16, 2021

Symptoms and severity: Not stated

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used RT-PCR

Genetic target: targeting the S gene; no further details provided

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Chu 2021 (b) (Continued)

	Assay used: As for reference sample		
	Genetic target: As for reference sample		
	Threshold: As for reference sample		
	Blinding reported: As for reference sample		
	Threshold predefined: As for reference sample		
	Index Sample (B): Nasal mid-turbinate		
	Sample collection device: Not stated		
	Sample collected by: Supervised patient		
	Sample collection method: Not stated		
	Sample storage/transport: Not stated		
	Timing of sample collection: Not stated		
	NAT extraction method: Not stated		
	Assay used: As for reference sample		
	Genetic target: As for reference sample		
	Threshold: As for reference sample		
	Blinding reported: As for reference sample		
	Threshold predefined: As for reference sample		
Target condition and reference standard(s)			
Flow and timing	Simultaneous sample collection: Unclear		
	Missing data: None reported		
	Uninterpretable results: None reported		
	Indeterminate results: None reported		
Comparative			
Notes	Funding: the Wellcome Trust		
	Publication status: Published correspondence		
	Source: Lancet Infectious Diseases		
	Author COI: CM, HC, CW, DH, and AB report grants from the Wellcome Trust during the conduct of the study. CYC declares no competing interests.		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Chu 2021 (b) (Continued)

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Unclear
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
If a threshold was used, was it pre-specified?	Unclear
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes

Chu 2021 (b) (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Congrave-Wilson 2021

Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals exposed to a household member with RT-PCR-confirmed SARS-CoV-2 within 2 weeks
	Recruitment: "Convenience sample"; contact tracing investigation?
	Prospective or retrospective: Unclear
	Sample size (cases): 889 (584)
	Additional inclusion criteria: 889 samples from 404 participants, repeated samples every 3-7 days up to 4 weeks or until 2 negative NP results

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Congrave-Wilson 2021 (Continued)

Patient characteristics and setting

Setting: Mixed: Hospital and community testing centres

Location: Children's Hospital Los Angeles

Country: USA

Dates: June 17, 2020 to February 15, 2021

Symptoms and severity: 93/404 (36.3%) asymptomatic, 126/404 (31.1%) reported mild severity

Demographics: Mean age (range): 28.2 (3.0-84.5)
108/404 (42.2%) male

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: 3 mL tube containing universal transport media

Sample collected by: Healthcare worker

Sample collection method: Study staff obtained the nasopharyngeal swab specimen following CDC guidelines; no details provided

Sample storage/transport: UTM. Samples were sent to the laboratory within 1 hour of collection.

Timing of sample collection: Samples were collected every 3 to 7 days for up to 4 weeks or until 2 negative nasopharyngeal test results.

NAT extraction method: QIAamp Viral RNA Mini Kit (QIAGEN, Valencia, CA)

Assay used: CDC protocol for RT-PCR

Genetic target: N1 and N2 genes

Threshold: Cycle threshold (Ct) value less than 40 for both N1 and N2

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: 50 mL sterile container

Sample collected by: Unsupervised patient

Sample collection method: Participants self-collected 3 mL saliva by allowing saliva to collect in the mouth and then dribbling or gently spitting into a 50 mL sterile container. They were also instructed not to cough or clear their throat while providing saliva samples to avoid contamination with excessive mucus.

Sample storage/transport: No preservative was added. Samples were sent to the laboratory within 1 hour of collection.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Congrave-Wilson 2021 (Continued)

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: The National Institutes of Health/National Institute of Allergy and Infectious Diseases

Publication status: Published paper

Source: JAMA

Author COI: Dr Pannaraj reported receiving consultant fees from Sanofi-Pasteur and Seqirus, research funding from Pfizer and AstraZeneca for unrelated studies, and grants from MedImmune. No other disclosures were reported.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		

Congrave-Wilson 2021 (Continued)

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	No
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes

Congrave-Wilson 2021 (Continued)

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias?

High risk

Cradic 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and OP and nasal anterior samples for the diagnosis of COVID-19; 182 (12) symptomatic patients suspected of COVID-19 meeting criteria for testing Recruitment: NP swab collection intended for routine testing; OP and nasal samples collected from patients who consented to subsequent additional sample collection. Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Emergency Department Location: OhioHealth Riverside Methodist Hospital. Ohio Health laboratories Country: USA Dates: Symptoms and severity: All patients symptomatic Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: HCW Sample collection method: Flocked swabs were used to collect nasopharyngeal specimens Sample storage/transport: Swabs were placed into 3 mL of sterile UVT (Becton Dickinson). Specimens were tested as soon as possible after collection, or if testing was delayed, were stored for up to 72 hours at 2 °C to 8 °C. Timing of sample collection: not stated NAT extraction method: Not stated. Assay used: Abbott ID NOW COVID-19 assay (Abbott Diagnostics) Genetic target: RdRp Threshold: Not stated Blinding reported: Not stated Threshold predefined: Not stated

Cradic 2020 (Continued)

Index Sample [A]: Oropharyngeal (OP)

Sample collected by: HCW

Sample collection method: Dry swab; no further details

Sample storage/transport:

Swabs were placed into 3 mL of sterile UVT (Becton Dickinson). Specimens were tested as soon as possible after collection, or if testing was delayed, were stored for up to 72 hours at 2 °C to 8 °C.

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used:

Abbott ID NOW COVID-19 assay (Abbott Diagnostics)

Genetic target: RdRp

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample [B]: anterior nasal

Sample collected by: HCW

Sample collection method: Dry swab collected according to CDC instructions using a single swab to sample both nares

Sample storage/transport:

Swabs were placed into 3 mL of sterile UVT (Becton Dickinson). Specimens were tested as soon as possible after collection, or if testing was delayed, were stored for up to 72 hours at 2 °C to 8 °C.

Timing of sample collection: Not stated

NAT extraction method: Not stated.

Assay used:

Abbott ID NOW COVID-19 assay (Abbott Diagnostics)

Threshold: Not stated

Genetic target: RdRp

Blinding reported: Not stated

Threshold predefined: Not stated

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Simultaneous

All patients received all sampling methods: Yes

Missing data: None reported

Cradic 2020 (Continued)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: None stated

Publication status: Published paper

Source: American Journal of Clinical Pathology

Author COI: None stated

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		

Cradic 2020 (Continued)

Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Collection method)		
DOMAIN 2: Index test (Oropharyngeal/nasal)		
DOMAIN 2: Index test (Nasal)		
If a threshold was used, was it pre-specified?	Yes	
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear	
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes	
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear	
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Oral rinse)		
DOMAIN 2: Index test (Operator)		
DOMAIN 3: Reference standard		
Could the reference standard, its conduct, or its interpretation have introduced bias?		
Are there concerns that the target condition as defined by the reference standard does not match the question?		
DOMAIN 4: Flow and timing		
Was there an appropriate interval between index tests?	Yes	
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes	
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes	
Were results presented per patient?	Yes	

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Cradic 2020 (Continued)

Were all patients included in the analysis?

Unclear

Could the patient flow have introduced bias?

Unclear risk

Da Costa Fernandes 2021
Study characteristics

Patient Sampling

Design: Single-group study
Patients oriented to perform the detection of SARS-CoV-2 either because of either having experienced high-risk contacts with positive COVID-19 patients or because of showing symptoms potentially indicative of COVID-19.

Recruitment: Unclear (452 samples were collected for the present work between 14th December 2020 and 27th January 2021)

Prospective or retrospective: Unclear, probably prospective

Sample size (cases):

(a) 226 (84) (no RNA extraction)

(b) 92 (76) (RNA extraction)

Patient characteristics and setting

Setting: Unclear

Location: ACES Cávado III Barcelos/Esposende

Country: Portugal

Dates: 14th December 2020 to 27th January 2021

Symptoms and severity: Not stated

Demographics:

Age: Not stated

Sex: 99/26 (39%) male

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Sterile tube containing 1 mL of sample preservation fluid (Biogen, China)

Sample collected by: Health care worker (HCW)

Sample collection method: NPS samples were collected with a sterile flocked swab placed in a sterile tube.

Sample storage/transport: 1 mL sample preservation fluid (Biogen,China). All samples were stored at 4 °C until processed. RNA was stored at -80 °C.

Timing of sample collection: Not stated

NAT extraction method: MagaBio plus Virus DNA/RNA purification kit II (BioFlux, Bioer, China)

Assay used: Novel Coronavirus (2019-nCoV) RT-PCR Detection Kit (Shanghai Fosun Long March Medical Science)

Da Costa Fernandes 2021 (Continued)

Genetic target: N, E and ORF1ab

Threshold: Ct ≤ 36 was defined as positive.

Blinding reported: Threshold predefined: Yes

Index Sample: Saliva drool

Sample collection device: Not stated

Sample collected by: Supervised patient/parent

Sample collection method: Saliva was collected by just letting the mouth's accumulated saliva drop into empty sterile sputum containers.

Sample storage/transport: As for index reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample threshold: As for reference sample

Blinding reported: As for reference sample threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by Project 72,545, 02/SAICT/2020, FEDER, Portugal 2020

Publication status: Published paper

Source: Journal of Clinical Virology

Author COI: Authors declared no COI present.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Was a case-control design avoided?

Yes

Did the study avoid inappropriate exclusions?

Unclear

Did the study avoid inappropriate inclusions?

Unclear

Da Costa Fernandes 2021 (Continued)

Was the intention that patients receive all tests at all time points? Yes

Could the selection of patients have introduced bias? Unclear risk

Are there concerns that the included patients and setting do not match the review question? Unclear

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Low risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

Da Costa Fernandes 2021 (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Unclear
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Da Silva 2022

Study characteristics

Patient Sampling	Design: Single-group study. Samples collected from symptomatic patients and asymptomatic patients who were in contact with either positive or suspected cases Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 61(19) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Regional Health Superintendence of Patos de Minas, Minas Gerais Country: Brazil Dates: August-September 2020 Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW Sample collection method: Not stated

Da Silva 2022 (Continued)

Sample storage/transport: Saline solution. All samples were kept in a cooler at 4 °C until processing in the laboratory

Timing of sample collection: Not stated

NAT extraction method: Bio Gene Kit from Bioclin

Assay used: RT-PCR Allplex™ 2019-nCov Assay (Seegene) kit

Genetic target: RdRP, N, and E genes

Threshold: At least one of the target genes amplified at Ct < 40

Blinding reported: Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Patients self-collected were 'guided' in collection of saliva samples in sterile containers.

Sample storage/transport: No medium. All samples were kept in a cooler at 4 °C until processing in the laboratory

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: Not stated

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear (probably yes)

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: Authors declared no COI present.

Methodological quality

Da Silva 2022 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			

Da Silva 2022 (Continued)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

De Oliveira 2021

Study characteristics

Patient Sampling	Design: Single group of adults (n = 403) seeking routine RT-PCR for SARS-CoV-2 Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 400 (157) Additional inclusion criteria: Table 4 provided info by time of symptoms onset; 2 x 2 table not extracted due to insufficient information
Patient characteristics and setting	Setting: Unclear Location: Santa Luzia Laboratory, Florianopolis, Santa Catarina State Country: Brazil Dates: October to November 2020 Symptoms and severity: 325/400 (81.2%) symptomatic Demographics: Not stated Exposure history: Not stated

De Oliveira 2021 (Continued)

Index tests

Reference sample: Mixed NP/OP

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: Two oro/nasopharyngeal swabs (ONS) were collected: one was introduced into the throat and scraped for 10 s and the second was into the nose and scraped for 10 s in each nostril.

Sample storage/transport: 3 mL of 0.9 % saline solution. Samples were frozen at -20 °C and sent to the Molecular Biology Department of Dasa Laboratories in Barueri, Brazil.

Timing of sample collection: Amongst the symptomatic patients (n = 325) the average time since symptoms onset was 5.04 (SD 2.95) days.

NAT extraction method: For LDT RT-PCR assay: Chemagen magnetic bead technology on the Chemagic™ 360 instrument (PerkinElmer, USA). For Abbott RT-PCR extraction, method not stated

Assay used: A lab-developed test (LDT) (n = 361), the Cobas® SARS-CoV-2 test in a Cobas 6800 system (Roche Diagnostics, USA) (n = 32) or the Abbott RealTime SARSCoV-2 assay (Abbott, USA) (n = 10)

Genetic target: For LDT: E gene

Other assays: Not stated

Threshold: The sample was considered positive for SARS-CoV-2 if two or more targets amplified or if only gene N amplified at a Ct threshold ≤ 40.

Blinding reported: Not stated

Threshold predefined: Not stated

Index sample: Saliva spit

Sample collection device: Dry sterile container

Sample collected by: Unsupervised patient/parent

Sample collection method: Patients were previously instructed to avoid drinking water for 10 min and refrain from other drinks, food, and nasal sprays for half an hour before sample collection. Patients received a dry sterile container and were asked to concentrate the saliva in their mouth and spit it (~1 mL) in the container and close it.

Sample storage/transport: Dry/direct sampling. Saliva specimens were thawed at room temperature, vortexed and a 50 µL aliquot was transferred to a 96 wells plate and 60 µg of proteinase K (New England Biolabs, USA) were added.

Timing of sample collection: As for reference sample

NAT extraction method: No RNA extraction

Assay used: TaqPath COVID-19 CE-IVD RT-PCR kit (ThermoFisher Scientific, USA)

Genetic target: T: S, N and ORF1ab genes

Threshold: The sample was considered positive for SARS-CoV-2 if two or more targets amplified or if only gene N amplified at a Ct threshold ≤ 40, as determined during our validation process. Samples in which only gene S or ORF1ab was positive, were considered negative for SARS-CoV-2.

Blinding reported: Not stated

De Oliveira 2021 (Continued)

Threshold predefined: Yes

Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: None reported Uninterpretable results: None reported Indeterminate results: 3 paired samples excluded due to saliva samples showing an invalid result
Comparative	
Notes	Funding: No funding Publication status: Published paper Source: Journal of Virological Methods Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		

De Oliveira 2021 (Continued)

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	No
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes

De Oliveira 2021 (Continued)

Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Desai 2021(a)[A]
Study characteristics

Patient Sampling	Design: Single group of 128 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing at the Wisconsin site Single group of 55 symptomatic COVID-19-confirmed positive patients admitted for observation and management at the New Jersey site (not extracted for this review) Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): From extracted 2 x 2 tables taking the sample pairs with the most D+ on either sample pair: 117 (16) Additional inclusion criteria: Samples from Rutgers New Jersey Medical School (NJMS), USA were excluded due to all patients being COVID-19 confirmed cases. 2 x 2 tables provided by authors (to CD - via email)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Medical College of Wisconsin (MCW), USA Country: USA Dates: December 2020 to April 2021 Symptoms and severity: No info provided Demographics: No info provided Exposure history: Not stated
Index tests	Index Sample (A): Nasal anterior nares Sample collection device: NS Sample collected by: Unsupervised patient Sample collection method: NS Sample storage/transport: Dry/ direct sampling. Samples frozen at -80 °C Timing of sample collection: Not stated NAT extraction method:

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Desai 2021(a)[A] (Continued)

	No RNA extraction
	Assay used: As for reference sample
	Genetic target: As for reference sample
	Threshold: As for reference sample
	Blinding reported: As for reference sample
	Threshold predefined: As for reference sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes
	Missing data: None reported
	Uninterpretable results: None reported
	Indeterminate results: 1.0% of NP, 1.4% of anterior nares, 3.9% of mid-turbinate, and 0% of saliva samples had invalid results.
Comparative	
Notes	Funding: Intramural NCI Cancer Moonshot and intramural research programme
	Publication status: Published paper
	Source: Microbiology Spectrum
	Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			

Desai 2021(a)[A] (Continued)

DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Desai 2021(a)[A] (Continued)

Could the patient flow have introduced bias?

High risk

Desai 2021(a)[B]
Study characteristics

Patient Sampling

Design: Single group of 128 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing at the Wisconsin site
Single group of 55 symptomatic COVID-19-confirmed positive patients admitted for observation and management at the New Jersey site (not extracted for this review)

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): From extracted 2 x 2 tables taking the sample pairs with the most D+ on either sample pair: 117 (16)

Additional inclusion criteria: Samples from Rutgers New Jersey Medical School (NJMS), USA were excluded due to all patients being COVID-19 confirmed cases.

2 x 2 tables provided by authors (to CD - via email)

Patient characteristics and setting

Setting: COVID-19 testing centre

Location: Medical College of Wisconsin (MCW), USA

Country: USA

Dates: December 2020 to April 2021

Symptoms and severity: No info provided

Demographics: No info provided

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal

Sample collection device: NS

Sample collected by: HCW

Sample collection method: NS

Sample storage/transport: [Dry/direct sampling. Samples frozen at -80 °C]

Timing of sample collection: Not stated

NAT extraction method: No RNA extraction

Assay used: The Atila iAMP test

Genetic target: N and ORF1ab genes

Threshold: Positive: if an exponential amplification curve with a cycle threshold (CT) of 50 was present in the FAM (ORF1ab or N genes) channel

Blinding reported: Not stated threshold predefined: Yes

Index Sample (B): Nasal mid-turbinate

Desai 2021(a)[B] (Continued)

Sample collection device: NS

Sample collected by: Unsupervised patient

Sample collection method: NS

Sample storage/transport: Dry/ direct sampling. Samples frozen at -80 °C

Timing of sample collection: Not stated

NAT extraction method:
No RNA extraction

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing	Simultaneous sample collection: Yes Missing data: None reported Uninterpretable results: None reported Indeterminate results: 1.0% of NP, 1.4% of anterior nares, 3.9% of mid-turbinate, and 0% of saliva samples had invalid results.

Comparative

Notes	Funding: Intramural NCI Cancer Moonshot and intramural research programme Publication status: Published paper Source: Microbiology Spectrum Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		

Desai 2021(a)[B] (Continued)

Was the intention that patients receive all tests at all time points? Unclear

Could the selection of patients have introduced bias? Unclear risk

Are there concerns that the included patients and setting do not match the review question? Unclear

DOMAIN 2: Index test (Saliva)
DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing
The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Desai 2021(a)[B] *(Continued)*

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Desai 2021(a)[C]
Study characteristics

Patient Sampling	Design: Single group of 128 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing at the Wisconsin site Single group of 55 symptomatic COVID-19-confirmed positive patients admitted for observation and management at the New Jersey site (not extracted for this review) Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): From extracted 2 x 2 tables taking the sample pairs with the most D+ on either sample pair: 117 (16) Additional inclusion criteria: Samples from Rutgers New Jersey Medical School (NJMS), USA were excluded due to all patients being COVID-19 confirmed cases. 2 x 2 tables provided by authors (to CD - via email)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Medical College of Wisconsin (MCW), USA Country: USA Dates: December 2020 to April 2021 Symptoms and severity: No info provided Demographics: No info provided Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal Sample collection device: NS Sample collected by: HCW

Desai 2021(a)[C] (Continued)

Sample collection method: NS

Sample storage/transport: [Dry/direct sampling. samples frozen at -80 °C

Timing of sample collection: Not stated

NAT extraction method: No RNA extraction

Assay used: The Atila iAMP test

Genetic target: N and ORF1ab genes

Threshold: Positive: if an exponential amplification curve with a cycle threshold (CT) of 50 was present in the FAM (ORF1ab or N genes) channel

Blinding reported: Not stated threshold predefined: Yes

Index Sample (C): Saliva nos

Sample collection device: NS

Sample collected by: Unsupervised patient

Sample collection method: NS

Sample storage/transport: Dry/direct sampling. Samples frozen at -80 °C

Timing of sample collection: Not stated

NAT extraction method:

No RNA extraction

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 1.0% of NP, 1.4% of anterior nares, 3.9% of mid-turbinate, and 0% of saliva samples had invalid results.

Comparative

Notes

Funding: Intramural NCI Cancer Moonshot and intramural research programme

Publication status: Published paper

Source: Microbiology Spectrum

Author COI: Authors declared no COI present.

Methodological quality

Desai 2021(a)[C] (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Desai 2021(a)[C] (Continued)

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Desai 2021(b)
Study characteristics

Patient Sampling	Design: Single group of 900 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing in the Salvador site and single group of 265 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing at the Paraguay site (analysed together) Single group of 55 symptomatic COVID-19 confirmed positive patients admitted for observation and management at the New Jersey site (not extracted for this review) Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): From extracted 2 x 2 tables taking the sample pairs with the most D+ on either sample pair: 1153 (230) Additional inclusion criteria: Samples from Rutgers New Jersey Medical School (NJMS), USA were excluded due to all patients being COVID-19 confirmed cases. 2 x 2 tables provided by authors (to CD - via email)
Patient characteristics and setting	Setting: COVID-19 testing centre

Desai 2021(b) (Continued)

Location: Hospital Nacional de Santa Ana, El Salvador and Hospital Materno Infantil de San Lorenzo, Ministerio de Salud Pública (MSP-BS), Paraguay

Country: El Salvador and Paraguay

Dates: December 2020 to April 2021

Symptoms and severity: [El Salvador] 272/900 (30.2%) symptomatic
[Paraguay] 207/265 (78.1%) symptomatic
[a] No info provided

Demographics:

[El Salvador]

Age:

18-28 y: 204/900 (22.7%);

29-39 y: 242/900 (26.9%);

40-50 y: 222/900 (24.7%);

≥ 50 y: 232/900 (25.8%);

Sex: 425/900 (47.2%) male

[Paraguay]

Age

18-28 y: 118/265 (44.5%);

29-39 y: 74/265 (27.9%);

40-50 y: 41/265 (15.5%);

≥ 50 y: 32/265 (21.1%);

Sex: 106/265 (40%) male

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal

Sample collection device: NS

Sample collected by: HCW

Sample collection method: NS

Sample storage/transport: [El Salvador] Dry/direct sampling no further details
[Paraguay] VTM samples frozen at -20 °C

Timing of sample collection: [El Salvador] Same day [Paraguay] NS

NAT extraction method: No RNA extraction

Assay used: The Atila iAMP test Genetic target: N and ORF1ab genes

Threshold: Positive: if an exponential amplification curve with a cycle threshold (CT) of 50 was present in the FAM (ORF1ab or N genes) channel

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: NS

Sample collected by: Unsupervised patient

Sample collection method: NS

Sample storage/transport: As for reference sample

Timing of sample: As for reference sample

NAT extraction method: As for reference sample

Desai 2021(b) (Continued)

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 1.0% of NP, 1.4% of anterior nares, 3.9% of mid-turbinate, and 0% of saliva samples had invalid results.

Comparative

Notes

Funding: Intramural NCI Cancer Moonshot and intramural research programme

Publication status: Published paper

Source: Microbiology Spectrum

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Desai 2021(b) *(Continued)*

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No

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Desai 2021(b) (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Desmet 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and OP/Nasal swabs for COVID-19 Design: 36(35) patients presenting to the Emergency Department suspected of COVID-19, based on respiratory and inflammatory symptoms (36 of 41 available sample pairs included in study) <i>[2] Study also reported separately on a subgroup of patients from [1] admitted to hospital with highly-suspect clinical and radiological features of COVID-19 (28 (27)) not extracted for this review</i> Recruitment: [1] "Upon presentation at the ED, all patients with suspected COVID-19 in whom a NP test was indicated for diagnosis, were candidates..." Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Emergency Department Location: Ghent University Hospital, Belgium Country: Belgium Dates: April 7 to May 1, 2020 Symptoms and severity: All patients symptomatic with 'respiratory and inflammatory symptoms' 28/36 (78%) required hospitalisation Demographics: Median age 61 years; range 22-90 Sex: 21/36 (58%) male Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: Not stated Sample collection method: NP "flexible mini tip flocked swab" performed after OP/ N in order not to contaminate the mid turbinate part of the nose with viral material from the nasopharynx. Swabs rotated x 3 for 'optimal mucosal contact' Sample storage/transport: Amies transport medium or universal transport medium (UTM) Timing of sample collection: Upon admission to ED NAT extraction method: NucliSens easyMag RNA extraction (bioMérieux, Marcy-l'Etoile, France) Assay used: one-step rRT-PCR (Qiagen One Step RT-PCR kit, Qiagen, Hilden, Germany) Genetic target: Not stated

Desmet 2020 (Continued)

Threshold: Cycle threshold (Ct) value < 50

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Oropharyngeal/nasal mid-turbinate (OP/mid-turbinate)

Sample collected by: Not stated

Sample collection method: OP/N swab: "non-flexible flocked swab with normal tip" swab rubbed in the oropharyngeal space twice at both sides of the uvula and the same swab placed into both nasal cavities until resistance felt (supposed mid-turbinate). Swabs rotated x 3 for 'optimal mucosal contact'

Sample storage/transport: Amies transport medium

Timing of sample collection: Upon admission to ED

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Sequential sampling

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: Preprint server (MedRxiv)

Author COI: Authors declared no COI present.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Desmet 2020 (Continued)

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	

Desmet 2020 (Continued)

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point No

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Dumaresq 2021
Study characteristics

Patient Sampling	Design: Single group of asymptomatic and symptomatic individuals aged ≥ 6 years presenting to a drive-through test centre Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 1005 (129) Additional inclusion criteria: Authors stated that samples were from 987 unique participants; then 18 samples were repeated sampling
Patient characteristics and setting	Setting: COVID-19 drive-through centre Location: Not stated, Quebec Country: Canada Dates: October 8 to 23, 2020 Symptoms and severity: 633/1005 (63%) were symptomatic Demographics: Age: Median (range): 40 (6-91) Sex: NS Exposure history: Not stated

Dumaresq 2021 (Continued)

Index tests

Reference sample: Mixed OP/NP

Sample collection device: 15 mL centrifuge tube

Sample collected by: Healthcare worker

Sample collection method: The flocked swab was first used to swab the posterior oropharynx and the tonsillar arches, and then the same swab was inserted through one nostril parallel to palate until resistance was met or the distance was equivalent to the distance from the patient's ear to their nostril, rotated several times and left in place for 5–10 s prior to being removed.

Sample storage/transport: The ONPS was placed in a conical 15 mL centrifuge tube containing 3 mL of molecular water (PCR grade water). The specimens were refrigerated at the collection site and transported to the laboratory in insulated coolers with ice pack.

Timing of sample collection: Not stated

NAT extraction method: No RNA extraction Assay used: Allplex™ 2019-nCoV Assay kit on CFX96 Touch Real-Time PCR Detection System (Bio-Rad, Hercules, CA, USA)

Genetic target: E, RdRp and N genes

Threshold: Ct values; no details provided

Blinding reported: Threshold predefined: Not stated

Index Sample: Gargle with natural spring water

Sample collection device: 15 mL conical polypropylene centrifuge tube

Sample collected by: Supervised patient

Sample collection method: Subjects were then provided with 5 mL of natural spring water (Eska water, St-Mathieu-d'Harricana, Quebec, Canada or Naya water, Mirabel, Quebec, Canada) in a disposable soft plastic cup (Plastic Medicine Cups, AMG Medical, Montreal, Quebec, Canada) and instructed to rinse their mouth for 5 s, tilt their head back and gargle for 5 s, repeat this cycle once, expel the water back in the plastic cup and empty it in a 15 mL conical polypropylene centrifuge tube.

Sample storage/transport: Natural spring water. The specimens were refrigerated at the collection site and transported to the laboratory in insulated coolers with ice pack.

Timing of sample collection: NS

NAT extraction method: As for reference standard sample

Assay used: As for reference standard sample

Genetic target: As for reference standard sample

Threshold: As for reference standard sample

Blinding reported: As for reference standard sample

Threshold predefined: As for reference standard sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

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Dumaresq 2021 (Continued)

Indeterminate results: Results were invalid for 2.7% (27 of 1005) ONPS and for 0.9% (9 of 1005) gargles; results retested by a second RT-PCR (unclear if reflected in the first 2 x 2 table/[Figure 1](#))

Comparative

Notes

Funding: the Ministère de la Santé et des Services Sociaux de la province de Québec (reagents and equipment) and the Centre Intégré de Santé et de Services Sociaux de Chaudière-Appalaches (human and technical resources)

Publication status: Published paper

Source: Journal of Clinical Virology

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
If a threshold was used, was it pre-specified?	Unclear		
Is undergoing one sample type unlikely to influence the result of the other sample type?	No		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

Dumaresq 2021 (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	No
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	No

Dumaresq 2021 (Continued)

Could the patient flow have introduced bias?

High risk

Echavarria 2021
Study characteristics

Patient Sampling	Design: Single group of symptomatic patients presenting at the emergency room (ER) in CEMIC University Hospital from August to September 2020 Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 174 (64) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Emergency Department Location: CEMIC University Hospital Country: Argentina Dates: August to September 2020 Symptoms and severity: All patients symptomatic at testing 9/174 (5.2%) required hospitalisation 1/174 (0.5%) was admitted to the ICU Demographics: Median age (IQR): 38 (31-50) 70/174 (40.2%) male Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal Sample collection device: sterile tube Sample collected by: Healthcare worker Sample collection method: Not stated Sample storage/transport: 2 mL viral transport media (Minimun Essential Medium; Gibco). NPS and saliva samples were transported at room temperature to the laboratory within 2 h of sample collection. Timing of sample collection: The median time from the onset of symptoms to sample collection was 2 days (IQR, 1–4). NAT extraction method: Quick-RNA™ Viral Kit, Zymo Research Corp Assay used: Optimised in-house one-step realtime RT-PCR assay Genetic target: E gene Threshold: A positive result was considered when the human RNase gene or the internal amplification control were positive and the cycle threshold (Ct) value was less than 40. Blinding reported: Not stated

Echavarria 2021 (Continued)

Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: Plastic sterile container

Sample collected by: Unsupervised patient

Sample collection method: Patients were also instructed to collect saliva by themselves.

Sample storage/transport: Dry/direct sampling. Saliva samples were transported at room temperature to the laboratory within 2 h of sample collection.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Fondo para la Investigación Científica y Tecnológica (FONCYT)

Publication status: Published paper

Source: Journal of Medical Virology

Author COI: COI declared: Martin Stryjewski is a consultant to Basilea, a speaker for Pfizer and principal investigator in Argentina for NIH grant UM1AI104681. The rest of the authors had no conflict of interest.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		

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Echavarria 2021 (Continued)

Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	

Echavarria 2021 (Continued)

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Escobar 2021

Study characteristics

Patient Sampling

Design: Samples were collected from symptomatic and asymptomatic individuals and from people who were in close contact with COVID-19 confirmed cases or who were clinically suspicious presenting to hospital (ambulatory) or the community.

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): 127 (54)

Additional inclusion criteria: From the initial population (n = 127); no information was obtained from three patients (n = 3). Two of them were ineligible and the other one was finally included in the analysis.

Patient characteristics and setting

Setting: Mixed hospital (probably O-P) and community

Location: Multi-specialised Guillermo Grant Benavente Hospital (HGGB) and three Family Health Centers (Boca sur FHC, Lagunillas FHC, Víctor Manuel Fernández FHC), Concepción

Country: Chile

Dates: February 2021

Symptoms and severity: 111/127 (87.4%) symptomatic

Demographics: Age: Range 11-77
Sex: 68/127 (53.3%) male

Exposure history: 21/127 (16.5%) with known exposure to COVID-19 case

Escobar 2021 (Continued)

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: NPS collected after saliva. No further details.

Sample storage/transport: All specimens were transported and maintained between 2 and 8 °C until use within 24 h of collection after which they were stored at -20 °C.

Timing of sample collection: Not stated

NAT extraction method: ExiPrep 96 Viral DNA/RNA Kit, ExiPrep™ 96 Lite (BIONEER, Daejeon, South Korea)

Assay used: Threshold: TaqMan™ 2019-nCoV
Assay Kit v1 (Applied Biosystems, CA, USA)

Genetic target: N gene

Threshold: Ct value < 37 or two replicates with Ct values of 38 were considered positive

Blinding reported:

Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: As for reference sample

Sample collected by: Patient/parent

Sample collection method: The sample were obtained by self-sampling by the patient, who deposited a volume between 1 and 2 mL of saliva into a sterile nuclease-free 15 mL centrifuge tube. At least 30 min before sampling, each patient followed several specific guidelines:

(1) no ingested food or liquids, except water; (2) no gum chewing; (3) no smoking or use of any type of mouth spray; and (4) no teeth brushing, no mouthwash, or dental floss. In addition, the participant had to remove cosmetic products, such as lip balms, and/or creams, when applicable

Sample storage/transport: Dry/direct sampling. All specimens were transported and maintained between 2 and 8 °C until use within 24 h of collection after which they were stored at -20 °C.

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 2 ineligible (nos)

Escobar 2021 (Continued)

Uninterpretable results: Excluded samples (n = 2) due to lack of amplification internal control to reference methodology and lack of amplification internal control to candidate methodology

Indeterminate results: None reported

Comparative
Notes

Funding: Supported by Health Public Institute of Chile

Publication status: Published paper

Source: Frontiers in Public Health

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample	Unclear		

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Escobar 2021 (Continued)

type interpreted without knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias?

Unclear risk

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Felix 2022

Study characteristics

Patient Sampling	Design: Single group Symptomatic children with suspected COVID-19 Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 50 (10) Additional inclusion criteria: Typo in the total number of positive samples with NPS (n = 12 instead of n = 16)
Patient characteristics and setting	Setting: Unclear Location: Public healthcare services of Araraquara Country: Brazil Dates: Unclear Symptoms and severity: 46/50 (92%) symptomatic at time of testing Demographics: Median age: 10.24 ± 3.52 Sex: 23/50 (46%) male Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: NS Sample collected by: NS Presume HCW Sample collection method: NS Sample storage/transport: The saliva samples were immediately stored at 4 °C until being taken to the laboratory (< 48 hours) Timing of sample collection: Mean duration of pso 4.76 days (SD 1.31) NAT extraction method: Viral RNA mini kit (Qiagen, GE) Assay used: Altona RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Altona Diagnostics GmbH, Hamburg, Germany) Genetic target: S gene Threshold: Ct < 40 for positivity Blinding reported: Not stated Threshold predefined: Yes Index Sample: Saliva spit Sample collection device: NS Sample collected by: Patient/parent Sample collection method: Children were asked to spit into a sterile container for collection of about 1 mL of saliva

Felix 2022 (Continued)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	No
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Felix 2022 (Continued)

Were all patients included in the analysis?

Unclear

Could the patient flow have introduced bias?

Unclear risk

Fernandez-Gonzalez 2021(a)
Study characteristics

Patient Sampling

Design: Single group study of asymptomatic and symptomatic patients presenting for SARS-CoV-2 testing, as requested by their providers, at the facilities of three primary care centres

Recruitment: Consecutive

Prospective or retrospective: Prospective

Sample size (cases): [A] 229 (50) - saliva supervised collection
[B] 140 (27) - oropharyngeal washing
[C] 208 (42) - saliva self-collection

Additional inclusion criteria: Numerical information showed by saliva sample method: total saliva could be calculated (but over 575 samples). Partial info about sensitivity by symptom status (not extracted here)

Patient characteristics and setting

Setting: Community (primary care centre)

Location: Three primary care centres of the province of Alicante

Country: Spain

Dates: September 15 to October 29, 2020

Symptoms and severity: 336/577 (58.2%) symptomatic

Demographics: Age: Median (range): 39 (24-51)
Sex: 251/577 (43.5%) male

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swabs

Sample collection device: Not stated

Sample collected by: Healthcare worker (HCW)

Sample collection method: A flexible minitip swab was passed through the patient's nostril until the posterior nasopharynx was reached, left in place for several seconds to absorb secretions, and then slowly removed while rotating.

Sample storage/transport: 3 mL of sterile transport medium containing guanidine salt (Mole Bioscience, SUNGO Europe B.V., Amsterdam, Netherlands). Specimens were transported within 2 h of sample collection to the clinical microbiology laboratory; NP samples were analysed immediately.

Timing of sample collection: ("as requested by providers")

NAT extraction method: Chemagic 360 nucleic acid purification instrument (PerkinElmer España SL, Madrid, Spain)

Assay used: LightMix Modular SARS-CoV (COVID-19) E-gene kit; TIB Molbiol, Berlin, Germany; distributed by Roche

Fernandez-Gonzalez 2021(a) (Continued)

Genetic target: E gene

Threshold: CT value of ≤ 40

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (A): Saliva spit, supervised

Sample collection device: Collection pot

Sample collected by: Supervised patient

Sample collection method: Subjects were instructed to produce and pool saliva in their mouths for 1 to 2 min, moving the mouth and passing the tip of the tongue across the cheeks and gums, and then to repeatedly spit a minimum of 1 mL of saliva into the collection pot in the presence of a healthcare worker.

Sample storage/transport: 100 mL sterile empty container without transport medium. Samples were frozen (-20°C). Specimens were transported within 2 h of sample collection to the clinical microbiology laboratory; saliva samples were analysed within 2 weeks after collection.

Timing of sample collection: ("as requested by providers")

NAT extraction method: As for reference sample assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Fifty-four patients (median [Q1 to Q3] age, 5.8 [4 to 10] years; 44 children) were unable to provide saliva specimens, and 3 (0.5%) specimens had insufficient samples for laboratory analysis.

Uninterpretable results: None reported

Indeterminate results: [Table 3](#)

Comparative

Notes

Funding: Instituto de Salud Carlos III - Subdirección General de Evaluación y Fondo Europeo de Desarrollo Regional and Instituto de Salud Carlos III

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Fernandez-Gonzalez 2021(a) *(Continued)*
DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled? Yes

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Did the study avoid inappropriate inclusions? Yes

Was the intention that patients receive all tests at all time points? Yes

Could the selection of patients have introduced bias?

Low risk

Are there concerns that the included patients and setting do not match the review question?

Low concern

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Yes

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)

Fernandez-Gonzalez 2021(a) (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Fernandez-Gonzalez 2021(b)
Study characteristics

Patient Sampling	Design: Single group study of asymptomatic and symptomatic patients presenting for SARS-CoV-2 testing, as requested by their providers, at the facilities of three primary care centres
	Recruitment: Consecutive
	Prospective or retrospective: Prospective
	Sample size (cases): [A] 229 (50) - saliva supervised collection [B] 140 (27) - oropharyngeal washing [C] 208 (42) - saliva self-collection

Fernandez-Gonzalez 2021(b) (Continued)

Additional inclusion criteria: Numerical information showed by saliva sample method: total saliva could be calculated (but over 575 samples). Partial info about sensitivity by symptom status (not extracted here)

Patient characteristics and setting

Setting: Community (primary care centre)

Location: Three primary care centres in the province of Alicante

Country: Spain

Dates: September 15 to October 29, 2020

Symptoms and severity: 336/577 (58.2%) symptomatic

Demographics: Age: Median (range): 39 (24-51)

Sex: 251/577 (43.5%) male

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swabs

Sample collection device: Not stated

Sample collected by: Healthcare worker (HCW)

Sample collection method: A flexible minitip swab was passed through the patient's nostril until the posterior nasopharynx was reached, left in place for several seconds to absorb secretions, and then slowly removed while rotating.

Sample storage/transport: 3 mL of sterile transport medium containing guanidine salt (Mole Bioscience, SUNGO Europe B.V., Amsterdam, Netherlands). Specimens were transported within 2 h of sample collection to the clinical microbiology laboratory; NP samples were analysed immediately.

Timing of sample collection: ("as requested by providers")

NAT extraction method: Chemagic 360 nucleic acid purification instrument (PerkinElmer España SL, Madrid, Spain)

Assay used: LightMix Modular SARS-CoV (COVID-19) E-gene kit; TIB Molbiol, Berlin, Germany; distributed by Roche

Genetic target: E gene

Threshold: CT value of ≤ 40

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (B): Saliva spit, unsupervised

Sample collection device: Collection pot

Sample collected by: Unsupervised patient

Sample collection method: Saliva specimens were collected independently by the individual providing the sample, following written instructions.

Sample storage/transport: 100 mL sterile empty container without transport medium. Samples were frozen (-20°C). Specimens were transported within 2 h of sample collection to the clinical microbiology laboratory; saliva samples were analysed within 2 weeks after collection.

Timing of sample collection: ("as requested by providers")

Fernandez-Gonzalez 2021(b) (Continued)

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Fifty-four patients (median [Q1 to Q3] age, 5.8 [4 to 10] years; 44 children) were unable to provide saliva specimens, and 3 (0.5%) specimens had insufficient samples for laboratory analysis.

Uninterpretable results: None reported

Indeterminate results: [Table 3](#)

Comparative

Notes

Funding: Instituto de Salud Carlos III - Subdirección General de Evaluación y Fondo Europeo de Desarrollo Regional and Instituto de Salud Carlos III

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Fernandez-Gonzalez 2021(b) (Continued)

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Yes

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

Fernandez-Gonzalez 2021(b) *(Continued)*

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Fernandez-Gonzalez 2021 (c)
Study characteristics

Patient Sampling	Design: Single group study of asymptomatic and symptomatic patients presenting for SARS-CoV-2 testing, as requested by their providers, at the facilities of three primary care centres Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): [A] 229 (50) - saliva-supervised collection [B] 140 (27) - oropharyngeal washing [C] 208 (42) - saliva self-collection Additional inclusion criteria: Numerical information showed by saliva sample method: total saliva could be calculated (but over 575 samples). Partial info about sensitivity by symptom status (not extracted here)
Patient characteristics and setting	Setting: Community (primary care centre) Location: Three primary care centres in the province of Alicante Country: Spain Dates: September 15 to October 29, 2020 Symptoms and severity: 336/577 (58.2%) symptomatic Demographics: Age: Median (range): 39 (24-51) Sex: 251/577 (43.5%) male Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swabs Sample collection device: Not stated Sample collected by: Healthcare worker (HCW)

Fernandez-Gonzalez 2021 (c) *(Continued)*

Sample collection method: A flexible minitip swab was passed through the patient's nostril until the posterior nasopharynx was reached, left in place for several seconds to absorb secretions, and then slowly removed while rotating.

Sample storage/transport: 3 mL of sterile transport medium containing guanidine salt (Mole Bioscience, SUNGO Europe B.V., Amsterdam, Netherlands). Specimens were transported within 2 h of sample collection to the clinical microbiology laboratory; NP samples were analysed immediately.

Timing of sample collection: ("as requested by providers")

NAT extraction method: Chemagic 360 nucleic acid purification instrument (PerkinElmer España SL, Madrid, Spain)

Assay used: LightMix Modular SARS-CoV (COVID-19) E-gene kit; TIB Molbiol, Berlin, Germany; distributed by Roche

Genetic target: E gene

Threshold: CT value of ≤ 40

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (C): Other: Oropharyngeal washing with saline

Sample collection device: collection pot

Sample collected by: Patient

Sample collection method: OPW consisting of rinsing the mouth with 2 mL of saline solution and spitting the solution into the collection pot

Sample storage/transport: 100 mL sterile empty container without transport medium. Samples were frozen (-20°C). Specimens were transported within 2 h of sample collection to the clinical microbiology laboratory.

Timing of sample collection: ("as requested by providers")

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Fifty-four patients (median [Q1 to Q3] age, 5.8 [4 to 10] years; 44 children) were unable to provide saliva specimens, and 3 (0.5%) specimens had insufficient samples for laboratory analysis.

Uninterpretable results: None reported

Indeterminate results: [Table 3](#)

Comparative

Fernandez-Gonzalez 2021 (c) (Continued)

Notes

Funding: Instituto de Salud Carlos III - Subdirección General de Evaluación y Fondo Europeo de Desarrollo Regional and Instituto de Salud Carlos III

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Fernandez-Gonzalez 2021 (c) *(Continued)*

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Fernández-Pittol 2020
Study characteristics
The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Fernández-Pittol 2020 (Continued)

Patient Sampling	Single-group study to compare agreement between OP/NP and saliva samples prepared using direct heat and separately with saliva samples prepared using RNA extraction Design: 51 (37) with laboratory or clinical radiologic findings compatible with a diagnosis of COVID-19: 'clinically diagnosed as having COVID-19'. Recruitment: Consecutive patients attending the Emergency Department Prospective or retrospective: Prospective Exclusion criteria: Patients presenting with infections or lesions in the oropharyngeal area were excluded.
Patient characteristics and setting	Setting: Accident and Emergency Location: Hospital Clinic of Barcelona Country: Spain Dates: Not stated Symptoms and severity: All patients (51) had laboratory or clinical radiologic findings compatible with a diagnosis of COVID-19. 28/51 (14%) < 9 days since the onset of symptoms Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Naso/oropharyngeal (NP/OP) Sample collected by: HCW Sample collection method: Swabs were 'deposited in a tube'. Sample storage/transport: Sample placed in 2 mL lysis buffer (guanidine thiocyanate, 2M; sodium citrate pH 7.0, 30 mM; dithiothreitol, 2 mM and triton X-100, 1%). The samples were transported to the Clinical Microbiology Department of the Hospital Clinic in Barcelona, Spain, within less than 2 hours after collection. Timing of sample collection: 28/51 < 9 days NAT extraction method: RNA was extracted from 500 µl of sample using a MagNA Pure Compact Instrument (Roche, Basel, Switzerland). Assay used: One step real time RT-PCR was performed using the RNA Process Control Kit (Roche, Basel, Switzerland) with 5 µl of extracted RNA. Genetic target: E Threshold: Not stated Blinding reported: Not stated Threshold predefined: Yes Index Sample: Saliva sample Sample collection device: (SARSTEDT, Germany) Sample collected by: Patient instructed and supervised by a HCW Sample collection method: All patients were asked to provide a saliva sample from the posterior oropharynx before toothbrushing and meal intake. Participants were asked

Fernández-Pittol 2020 (Continued)

to collect saliva in their mouth and to gently spit it by aid of a funnel in a sterile cryotube collection tube. Patients were instructed and supervised by HCW. Saliva samples with a volume less than 500 µL were not included in the study.

Sample storage/transport: The samples were transported to the Clinical Microbiology Department of the Hospital Clinic in Barcelona, Spain, within less than 2 hours after collection. All saliva samples were stored at –80 °C and processed together.

Timing of sample collection: As for Reference sample

NAT extraction method: 350 µL of saliva were mixed with 350 µL of lysis buffer (MagNA Pure Compact RNA Isolation Kit, Roche). RNA was extracted from 500 µL of sample using a MagNA Pure Compact Instrument (Roche, Basel, Switzerland) with an elution volume of 50 µL.

Assay used: As for Reference sample

Genetic target: As for Reference sample

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Unclear

Time interval between sampling methods: Unclear

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: preprint

Source: bioRxiv

Author COI: Not stated

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Yes

Was a case-control design avoided?

Yes

Did the study avoid inappropriate exclusions?

Unclear

Fernández-Pittol 2020 (Continued)

Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	

Fernández-Pittol 2020 (Continued)

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Unclear risk

FIND (a) 2021
Study characteristics

Patient Sampling	Design: Single-group adults in community meeting national COVID-19 suspect definition. No further details Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 218 (79) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Community clinic. Marica and Guapimirim, state of Rio de Janeiro Country: Brazil Dates: 21 to 27 January 2021 and 23 to 26 February 2021 Symptoms and severity: 218/218 (100%) symptomatic Demographics: Age: Mean (range) 42.3 (18-90)

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FIND (a) 2021 (Continued)

	Sex: 92/218 (42%) male
	Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: NowCheck COVID-19 Ag Test RG1901DG (NP) Bionote, Inc. Sample collected by: NS Sample collection method: NS Sample storage/transport: Test kit storage 2-30 °C. Timing of sample collection: Median(Q1-Q3): 4(3-6) NAT extraction method: NA NowCheck COVID-19 Ag Test; RG1901DG (NP) Assay used: Ag NowCheck COVID-19 Ag Test; RG1901DG (NP) Genetic target: Nucleocapsid antigen Threshold: Blinding reported: NS Threshold predefined: NS Index Sample: Nasal anterior nares Sample collection device: NowCheck COVID-19 Ag Test; RG1901DGN (Nasal), Bionote, Inc. Sample collected by: NS Sample collection method: NS Sample storage/transport: As for reference sample Timing of sample collection: As for reference sample NAT extraction method: NA Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: None reported Uninterpretable results: None reported

FIND (a) 2021 (Continued)

Indeterminate results: None reported

Comparative

Notes

Source: FIND

Author COI: None declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		

FIND (a) 2021 (Continued)

Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Oral rinse)		
DOMAIN 2: Index test (Operator)		
DOMAIN 3: Reference standard		
Could the reference standard, its conduct, or its interpretation have introduced bias?		
Are there concerns that the target condition as defined by the reference standard does not match the question?		
DOMAIN 4: Flow and timing		
Was there an appropriate interval between index tests?	Yes	
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Unclear	
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes	
Were results presented per patient?	Yes	
Were all patients included in the analysis?	Unclear	
Could the patient flow have introduced bias?		Unclear risk

FIND (b) 2021

Study characteristics	
Patient Sampling	Design: Single group of adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting the suspect definition of the Department of Public Health. No further details Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 281 (22) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Heidelberg

FIND (b) 2021 (Continued)

	Country: Germany Dates: 15 December 2020 to 19 January 2021 Symptoms and severity: Symptoms: 130/279 (46.2%) Demographics: Age: Mean (range): 42.9 (18-81) Sex: 134/280 (47.9%) male Exposure history: Not stated
Index tests	Reference sample: NPS Sample collection device: Panbio COVID-19 Ag Rapid Test Device Nasopharyngeal 41FK10 (nasopharyngeal evaluated) Sample collected by: NS Sample collection method: NS Sample storage/transport: Test kit storage 2-30 °C Timing of sample collection: Median (Q1-Q3): 3 (1-5) pso NAT extraction method: NA Assay used: Panbio COVID-19 Ag Rapid Test Device Nasopharyngeal 41FK10 (nasopharyngeal evaluated) Genetic target: Nucleocapsid antigen Threshold: Blinding reported: NS Threshold predefined: NS Index Sample: Nasal mid-turbinate Sample collection device: Panbio COVID-19 Ag Rapid Test Device Nasal 41FK11 (nasal version evaluated) Sample collected by: NS Sample collection method: NS Sample storage/transport: As for reference sample Timing of sample collection: As for reference sample NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes

FIND (b) 2021 (Continued)

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Source: FIND report

Author COI: None declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

FIND (b) 2021 (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

FIND (c) 2021(a)

Study characteristics	
Patient Sampling	Design: Adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting the suspect definition of the Department of Public Health Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 179 (42)
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through

FIND (c) 2021(a) (Continued)

	Location: Ambulatory testing clinic of Charité – University Hospital, Berlin Country: Germany Dates: 11-18 November 2020 Symptoms and severity: 173/179 (96.6%) Demographics: Age: Mean (range) 36.2 (18-72) Sex: 93/179 (52%) Exposure history: Not stated
Index tests	Reference sample: NPS Sample collection device: STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosensor, Inc. Sample collected by: NS Sample collection method: NS Sample storage/transport: Kit extraction buffer. Storage 2-30 °C Timing of sample collection: Median (Q1-Q3): 4(3-5) pso NAT extraction method: NA Assay used: STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosensor, Inc. Genetic target: Nucleocapsid antigen Threshold: Blinding reported: NS Threshold predefined: NS Reference sample: NPS Sample collection device: STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosensor, Inc. Sample collected by: NS Sample collection method: NS Sample storage/transport: Kit extraction buffer. Storage 2-30 °C Timing of sample collection: Median (Q1-Q3): 4(3-5) pso NAT extraction method: NA Assay used: STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosensor, Inc. Genetic target: Nucleocapsid antigen Threshold: Blinding reported: NS Threshold predefined: NS
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: None reported

FIND (c) 2021(a) (Continued)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Source: FIND report

Author COI: None declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

FIND (c) 2021(a) (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

FIND(c) 2021 (b)

Study characteristics

Patient Sampling	Design: Single group of adults in the community meeting national suspect definition for COVID-19 nos Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 214 (78)
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through

FIND(c) 2021 (b) *(Continued)*

Location: Community testing clinic, Marica and Guapimirim, state of Rio de Janeiro

Country: Brazil

Dates: 14-20 January 2021; 2-4 March 2021

Symptoms and severity: 214/214 (100%)

Demographics: Age: Mean (range) 41.31 (18-77)

Sex: 85/214 (40%)

Exposure history: Not stated

Index tests

Reference sample: NPS

Sample collection device: STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosensor, Inc.

Sample collected by: NS

Sample collection method: NS

Sample storage/transport: Kit extraction buffer. Kit storage 2-30 °C

Timing of sample collection: Median (Q1-Q3): 5(3-7) pso

NAT extraction method: NA

Assay used: Threshold: STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosensor, Inc.

Genetic target: Nucleocapsid antigen

Threshold: NS

Blinding reported: NS

Threshold predefined: NS

Index Sample: Nasal anterior nares

Sample collection device: STANDARD Q COVID-19 Ag Test 09COV31D.SD Biosensor, Inc.

Sample collected by: NS

Sample collection method: NS

Sample storage/transport: Kit extraction buffer

Timing of sample: As for reference sample

NAT extraction method: NA

Assay used: As for index reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

FIND(c) 2021 (b) *(Continued)*

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Source: FIND Report

Author COI: None declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		

FIND(c) 2021 (b) *(Continued)*

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

FIND(s) 2021

Study characteristics

Patient Sampling	Design: Single-group symptomatic adults presenting to a dedicated COVID-19 drive-through testing centre to determine the accuracy of COVID-19 antigen RDTs, using consecutive enrolment Recruitment: Consecutive Prospective or retrospective: Prospective

FIND(s) 2021 (Continued)

	Sample size (cases): 369 (121) (NPS RT-PCR reference standard)
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Liverpool John Lennon Airport Country: UK Dates: 14 October–16 September 2021 Symptoms and severity: Symptomatic: 369/369 (100%) Demographics: Age: Mean (range) 43 (18-831) Sex: 159/369 (43%) Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collected by: NS Sample collection method: NS Sample storage/transport: Test kit stored between 4 and 300 °C Timing of sample collection: Median days (Q1-Q3) pso: 2(1-3) NAT extraction method: NA Assay used: Sure Status® COVID-19 Antigen Card Test – Nasopharyngeal Swab Genetic target: Nucleocapsid antigen Threshold: NS Blinding reported: NS Threshold predefined: NS Index Sample: Nasal nos Sample collected by: NS Sample collection method: NS Sample storage/transport: As for reference sample Timing of sample collection: As for reference sample NAT extraction method: NA Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes

FIND(s) 2021 (Continued)

		Missing data: None reported	
		Uninterpretable results: 6 invalid nasal Ag (index) samples 1 invalid NPS Ag index reference sample	
		Indeterminate results: None reported	
Comparative			
Notes		Source: FIND report	
		Author COI: No COI reported	
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear		

FIND(s) 2021 (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Fougere 2021

Study characteristics

Patient Sampling	Design: Single group of children presenting with symptoms compatible with COVID-19 according to 'national guidelines'
	Recruitment: Unclear (children 1 month to 18 years of age were recruited from 2 different outpatient clinics in Lausanne). Children > 12 years had to report at least one major symptom (fever, respiratory symptoms such as cough, throat pain, dyspnoea or thoracic pain, anosmia, dysgeusia) or 1 minor symptom + contact with a confirmed COVID-19 case. Testing criteria were 'more strict' for children < 12 years (no further details).
	Prospective or retrospective: Prospective

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Fougere 2021 (Continued)

	Sample size (cases): 397(106) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital Outpatient Location: Multi-site: Montétan screening site, Department of Mother-Woman-Child, Lausanne University Hospital and Vidy-Med Pediatric Emergency Center, Lausanne Country: France Dates: Unclear Symptoms and severity: All (100%) symptomatic Demographics: Age: Mean 12.7 ± 3.8 Sex: 205/397 (52%) male Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: Health care worker (HCW) Sample collection method: Unclear Sample storage/transport: 3 mL VTM. Samples were sent the same day or the next morning. Timing of sample collection: Unclear; 'Only 3/397 patients were > 7 days pso' NAT extraction method: NS Assay used: Threshold: In-house RT-PCR on the automated molecular diagnostic platform targeting the E gene or using the SARS-CoV-2 test of the Cobas 6800 instrument (Roche, Basel, Switzerland) Genetic target: E gene not stated Threshold: The cycle threshold (cycle when the RT-PCR was positive, i.e., above the threshold of fluorescence) was provided automatically by the instruments using the default parameter. Blinding reported: NS Threshold predefined: Yes Index Sample: Saliva drool Sample collection device: Not stated Sample collected by: Patient or supervised patient/parent Sample collection method: Collection of a significant amount of saliva and the drooling of at least 10 µL of saliva in a tube when possible Sample storage/transport: As for reference sample Timing of sample collection: As for reference sample NAT extraction method: As for reference sample Assay used: As for index reference sample

Fougere 2021 (Continued)

Genetic target: Not stated

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 878 tested at setting, of which 405 included in this study. Results available for 397. No further details provided

At least 8 sample pairs had missing data.

Uninterpretable results: Not stated

Indeterminate results: Not stated

Comparative

Notes

Funding: Not stated

Publication status: Published paper

Source: Pediatric Infectious Disease Journal

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Fougere 2021 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	No
Were the proportions and reasons for missing data similar across sample types (index test)?	No

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Fougere 2021 (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Fronza 2021 (a)
Study characteristics

Patient Sampling	Design: Single group of individuals undergoing testing for having been recently in contact with infected persons (contact tracing), convalescent individuals tested to confirm their recovery, healthcare professionals for routine screening or symptomatic individuals suspected of infection Symptomatic n = 32 422 symptomatic convalescent and 336 asymptomatic screened HCW could not be disaggregated and so were not included in this review. Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 32 (15) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Drive-through testing facility, Trento Country: Italy Dates: March 25 to April 23, 2021 Symptoms and severity: 32/32 (100%) symptomatic Demographics: Age: Mean 41.7 (SD 15.2) Sex: 434/1003 (43%) male (included prior tested individuals not included in this review and the population from Fronza (b)) Exposure history: 193/1003 (19%) with known exposure to COVID-19 cases, 442/1003 (44%) with previous COVID-19 infection (included prior tested individuals not included in this review and the population from Fronza (b))
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: Healthcare worker (HCW) Sample collection method: Unclear Sample storage/transport: Both saliva and NP swabs were stored at 4 °C overnight. Samples were transported to the laboratory the same day and processed for analysis the following day. Timing of sample collection: Not stated

Fronza 2021 (a) (Continued)

NAT extraction method: MagMAX Viral/Pathogen Nucleic Acid Isolation Kit (ThermoFisher)

Assay used: Novel Coronavirus Real Time Multiplex RT-PCR Kit (Liferiver)

Genetic target: RdRp gene

Threshold: Ct > 40 for positivity

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: Saliva collection kit (Comedical, Trento, Italy)

Sample collected by: Unsupervised patient/parent

Sample collection method: Individuals collected the saliva autonomously after reading or watching the instructions linked with the kit (<https://www.covidsaliva.it/>).

Inclusion in the study required not having eaten, drunk or smoked for at least 30 minutes prior to saliva collection.

Sample storage/transport: Saliva samples were fluidified with the addition of 1 mL DTT 6.5 mM in water.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 22/1025 (2%) tubes containing visibly less than 0.5 mL of oral fluid (saliva) were excluded.

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Funding from PAT (Provincia Autonoma di Trento) to the University of Trento with a contribution from APSS (Azienda Provinciale per i Servizi Sanitari, Trento) and from the University of Trento

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Fronza 2021 (a) (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			

Fronza 2021 (a) *(Continued)*
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Fronza 2021 (b)
Study characteristics

Patient Sampling	Design: Single group of individuals undergoing testing for having recently been in contact with infected persons (contact tracing), convalescent individuals tested to confirm their recovery, healthcare professionals for routine screening or symptomatic individuals suspected of infection [b] Asymptomatic contact tracing n = 193 422 asymptomatic convalescent and 336 asymptomatic screened HCW could not be disaggregated and so were not included in this review. Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 193 [77] Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through

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Fronza 2021 (b) (Continued)

Location: Drive-through testing facility, Trento

Country: Italy

Dates: March 25 to April 23, 2021

Symptoms and severity: 0/193 (0%) symptomatic

Demographics: Age: Mean 41.7 (SD 15.2)

Sex: 434/1003 (43%) male

(Included prior tested individuals not included in this review and population from Fronza (a))

Exposure history: 193/1003 (19%) with known exposure to COVID-19 cases, 442/1003 (44%) previous COVID-19 infection

(Included prior tested individuals not included in this review and population from Fronza (a))

Index tests
Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: Health care worker (HCW)

Sample collection method: Unclear

Sample storage/transport: Both saliva and NP swabs were stored at 4 °C overnight. Samples were transported to the laboratory the same day and processed for analysis the following day.

Timing of sample collection: Not stated

NAT extraction method: MagMAX Viral/Pathogen Nucleic Acid Isolation Kit (ThermoFisher)

Assay used: Novel Coronavirus Real Time Multiplex RT-PCR Kit (Liferiver)

Genetic target: RdRp gene

Threshold: Ct > 40 for positivity

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: Saliva collection kit (Comedical, Trento, Italy)

Sample collected by: Unsupervised patient/parent

Sample collection method: Individuals collected the saliva autonomously after reading or watching the instructions linked with the kit (<https://www.covidsaliva.it/>).

Inclusion in the study required not having eaten, drunk or smoked for at least 30 minutes prior to saliva collection.

Sample storage/transport: Saliva samples were fluidified with the addition of 1 mL DTT 6.5 mM in water.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Fronza 2021 (b) (Continued)

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)
Flow and timing

Simultaneous sample collection: Yes

Missing data: 22/1025 (2%) tubes containing visibly less than 0.5 mL of oral fluid (saliva) were excluded.

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative
Notes

Funding: Funding from PAT (Provincia Autonoma di Trento) to the University of Trento with a contribution from APSS (Azienda Provinciale per i Servizi Sanitari, Trento) and from the University of Trento

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Fronza 2021 (b) *(Continued)*

Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point?	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Fronza 2021 (b) *(Continued)*

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Goncalves 2021
Study characteristics

Patient Sampling	Design: Unclear group of mild-symptomatic and asymptomatic subjects tested in Rio de Janeiro state Recruitment: Unclear Prospective or retrospective: Unclear Sample size (cases): [A] 157 (27) for the oral gingival swab group [B] 207 (85) for the saliva spit group Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed hospital outpatient and COVID-19 testing centre Location: Marcílio Dias Naval Hospital (HNMD), the COVID-19 Diagnostic Centre of the Federal University of Rio de Janeiro, and the COVID-19 diagnosis tents in the Maricá municipality Country: Brazil Dates: Not stated Symptoms and severity: [A] 6/158 (3.82%) asymptomatic Mean days from the onset of symptoms to sample collection: 4.71 ± 2.37 [B] 38/207 (18.36%) asymptomatic Mean days from the onset of symptoms to sample collection: 7.11 ± 11.39 Demographics: [A] Age: Mean (SD): 39 ± 13 y Sex: 150/158 (31.6%) males [B] Age: Mean (SD): 43 ± 15.5 y Sex: 109/207 (52.6%) male Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal Sample collection device: tube containing 2 mL of viral transport medium (VTM) Sample collected by: Healthcare worker Sample collection method: NP swab collection was performed by introducing a rayon-tipped swab into the nasal cavity, directing it upwards (towards the eyes), at an angle of 30° to 45° in relation to the upper lip. The swab was rotated 10 times while in the NP cavity, and allowed to rest for 30 seconds prior to removal.

Goncalves 2021 (Continued)

Sample storage/transport: VTM

Timing of sample collection: Not stated

NAT extraction method: Maxwell®16 Viral Total Nucleic Acid Purification Kit (Promega)

Assay used: SARS-CoV-2 (2019-nCoV) CDC qPCR Probe Assay (Integrated DNA Technologies, IA, USA)

Genetic target: N1 and N2 genes

Threshold: both targets (N1 and N2) amplified with cycle threshold (Ct) ≤ 37

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (A): Oral (gingival fluid)

Sample collection device: A tube with VTM

Sample collected by: Not stated

Sample collection method: A rayon-tipped swab was rubbed against both the maxillary and the mandibular gingiva. After rubbing both right and left sides, the swab was placed in a tube with 2 mL of VTM.

Sample storage/transport: VTM

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Index Sample (B): Saliva spit

Sample collection device: A sterile receptacle

Sample collected by: Unsupervised patients

Sample collection method: Patients were asked to spit into a sterile recipient, producing at least 1 mL of saliva.

Sample storage/transport: Dry/direct sample

Timing of sample collection: Samples were kept refrigerated until further analysis.

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Goncalves 2021 (Continued)

Threshold predefined: As for reference sample

Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: None reported Uninterpretable results: None reported Indeterminate results: 1 and 3 inconclusive NP samples
Comparative	
Notes	Funding: FAPERJ, CAPES, Instituto Serrapilheira Publication status: Published paper Source: Mem Inst Oswaldo Cruz Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted	Unclear		

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Goncalves 2021 (Continued)

without knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Yes

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Goncalves 2021 (Continued)

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Griesemer 2021 (a)
Study characteristics

Patient Sampling	Design: Single group of patients for COVID-19 testing; without an appointment and also without the requirement of being symptomatic from Albany Medical Center (AMC) Emergency Department parking lot (n = 236) Recruitment: Unclear (collected between 20 and 26 March 2020) Prospective or retrospective: Prospective Sample size (cases): 236 (12) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Emergency Department Location: Medical Center (AMC) Emergency Department, Albany Country: USA Dates: Between 20 and 26 March 2020 Symptoms and severity: Not stated Demographics: Age: Range 3-105 Sex: 111/236 (47%) male Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Tubes with molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX) Sample collected by: Unclear (probably HCW) Sample collection method: Flocked NPS swabs were inserted in the NP cavity to approximately 1 inch and gently rotated for 10 to 15 s. Samples were introduced in tubes containing 1 mL molecular transport medium.

Griesemer 2021 (a) (Continued)

Sample storage/transport: Molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX). Those from NR were placed in coolers and transported to the LVD within 24 h for accessioning and testing. Specimens were held at 4 °C from collection to processing into lysis buffer for molecular testing.

Timing of sample collection: Not stated. All testing was performed within 24 to 72 h of the time of specimen collection.

NAT extraction method: bioMérieux easyMAG or EMAG (bioMérieux Inc, Durham, NC) MagNA Pure 96 system (Roche Diagnostics, Indianapolis, IN)

Assay used: CDC 2019 nCoV real-time reverse transcription-PCR (RT-PCR) diagnostic panel

Genetic target: N1 gene

Threshold: Ct < 40 (<https://www.fda.gov/media/134922/download>)

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample (A): Nasal swab

Sample collection device: Tubes with molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)

Sample collected by: Unclear (probably HCW)

Sample collection method: Collection of NS was by bilateral swabbing on flocked swabs with insertion to approximately one inch and gentle rotation for several seconds.

Samples were introduced in tubes containing 1 mL molecular transport medium.

Sample storage/transport: Molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: Not stated

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Index Sample (B): Saliva drool

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Patients were instructed to refrain from eating, drinking, chewing gum or tobacco, or smoking for 30 min prior to collection and to work up saliva in their mouth, not cough, and to drool or gently spit the saliva into the container. Collected in sterile 50 mL conical tubes

Sample storage/transport: Direct sampling

Timing of sample collection: As for reference sample

Griesemer 2021 (a) (Continued)

NAT extraction method: As for reference sample

Assay used: Not stated

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Performed with internal funding from the NYSDOH and AMC

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: S.B.G., G.V.S., D.E., T.Y., D.A.C., A.C.W., A.K.C., and M.J.W. declare no conflict of interest. K.S. has served as a paid consultant for T2 Biosystems and Roche Diagnostics. K.S.G. receives research support from ThermoFisher for the evaluation of new assays for the diagnosis and characterisation of viruses, including SARS-CoV-2. She also has a royalty-generating collaborative agreement with Zeptomatrix.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern

Griesemer 2021 (a) *(Continued)*
DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

DOMAIN 2: Index test (Oral rinse)
The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Griesemer 2021 (a) *(Continued)*
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Griesemer 2021 (b)
Study characteristics

Patient Sampling	Design: Single group of patients for COVID-19 testing: with the requirement of having an appointment and qualifying symptoms or exposures, from drive-through Regional Operations Center (ROC) in New Rochelle (n = 227) Recruitment: Unclear (collected between 20 and 26 March 2020) Prospective or retrospective: Prospective Sample size (cases): 227 (93) Additional inclusion criteria:
Patient characteristics and setting	Setting: COVID-19 test centre/drive-through Location: Drive-through Regional Operations Center (ROC), New Rochelle, New York Country: USA Dates: Between 20 and 26 March 2020 Symptoms and severity: Not stated

Griesemer 2021 (b) (Continued)

Demographics: Age: Range 14-77

Sex: 136/227 (60%) male

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Tubes with molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)

Sample collected by: Unclear (probably HCW)

Sample collection method: Flocked NPS swabs were inserted in the NP cavity to approximately 1 inch and gently rotated for 10 to 15 s

Samples were introduced in tubes containing 1 mL molecular transport medium.

Sample storage/transport: Molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX). Those from NR were placed in coolers and transported to the LVD within 24 h for accessioning and testing. Specimens were held at 4 °C from collection to processing into lysis buffer for molecular testing.

NAT extraction method: All testing was performed within 24 to 72 h of the time of specimen collection.

Timing of sample collection: Not reported

NAT extraction method: BioMérieux easyMAG or EMAG (bioMérieux Inc, Durham, NC) MagNA Pure 96 system (Roche Diagnostics, Indianapolis, IN)

Assay used: CDC 2019 nCoV real-time reverse transcription-PCR (RT-PCR) diagnostic panel

Genetic target: N1 gene

Threshold: Ct < 40 (<https://www.fda.gov/media/134922/download>)

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Nasal swab

Sample collection device: Tubes with molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)

Sample collected by: Unclear (probably HCW)

Sample collection method: Collection of NS was by bilateral swabbing on flocked swabs with insertion to approximately one inch and gentle rotation for several seconds

Samples were introduced in tubes containing 1 mL molecular transport medium.

Sample storage/transport: Molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: Not stated

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Griesemer 2021 (b) (Continued)

Threshold predefined: As for reference sample

Index Sample (B): Saliva drool

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Patients were instructed to refrain from eating, drinking, chewing gum or tobacco, or smoking for 30 min prior to collection and to work up saliva in their mouth, not cough, and to drool or gently spit the saliva into the container. Collected in sterile 50 mL conical tubes.

Sample storage/transport: Direct sampling

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Performed with internal funding from the NYSDOH and AMC

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: S.B.G., G.V.S., D.E., T.Y., D.A.C., A.C.W., A.K.C., and M.J.W. declare no conflict of interest. K.S. has served as a paid consultant for T2 Biosystems and Roche Diagnostics. K.S.G. receives research support from ThermoFisher for the evaluation of new assays for the diagnosis and characterisation of viruses, including SARS-CoV-2. She also has a royalty-generating collaborative agreement with Zeptomatrix.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		

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Griesemer 2021 (b) *(Continued)*

Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes

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Griesemer 2021 (b) *(Continued)*

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?

Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?

Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point

Yes

Were the proportions and reasons for missing data similar across sample types (index test)?

Yes

Were results presented per patient?

Yes

Were all patients included in the analysis?

Unclear

Could the patient flow have introduced bias?

Unclear risk

Guclu 2020 (a)
Study characteristics

Patient Sampling

Single-group study to estimate agreement between NP/OP and saliva samples for the diagnosis of COVID-19

Design: 15 (5) inpatients admitted from A&E (day 0) with normal CT but signs and symptoms compatible with COVID-19

Guclu 2020 (a) (Continued)

[See [Guclu 2020 \(b\)](#) for report of two-group study of symptomatic patients with (30) and without (19) PCR-confirmed COVID infection]

Recruitment: Not stated

Prospective or retrospective: Prospective

Patient characteristics and setting

Setting: A&E department

Location: Sakarya University Training and Research Hospital

Country: Turkey

Dates: Not stated

Symptoms and severity: Symptomatic patients (fever, cough, shortness of breath) but normal CT findings

Demographics: Info provided for all 64 participants contributing to [Guclu 2020 \(a\)](#) and [Guclu 2020 \(b\)](#) combined:

Mean age: 51 ± 17.9 years

Male: 37/64 (57.8%)

Exposure history: Not stated

Index tests

Reference Sample: Naso/oropharyngeal (NP/OP)

Sample collected by: HCW

Sample collection method: Dacron-flocked swab inserted first into the posterior oropharynx and the posterior pharynx was swabbed for 2-3 seconds. The swab was then inserted through the nostril with a rotation movement until the nasopharynx was reached and the sample was obtained by rotating the swab gently for 2-3 seconds. Swab then placed into a 5 mL tube containing 2 mL viral transport medium (VTM)

Sample storage/transport: VTM; samples were delivered to the lab within one hour.

Timing of sample collection: At the time of hospital admission

NAT extraction method: EZ1 (Qiagen, Germany) device

Assay used: genesis RT-PCR SARS-COV-2 (Primer Design, UK) kit

Genetic target: Not stated

Threshold: Ct value < 45

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Patients were asked to collect the saliva sample themselves. They were given a sterile dry container and told to close the lid of the container after placing the saliva in it.

Sample storage/transport: Direct samples were delivered to the lab within one hour.

Guclu 2020 (a) (Continued)

Data 2019 (4) (continued)

	Timing of sample collection: At the time of hospital admission NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: Not stated Threshold: As for reference sample Blinding reported: Not stated Threshold predefined: Yes		
Target condition and reference standard(s)			
Flow and timing	Sampling schedule prespecified: Yes: Paired samples; second swab was taken on patients with a negative first sample. Time interval between sampling methods: Simultaneous All patients received all sampling methods: Yes Missing data: None reported Uninterpretable results: None reported Indeterminate results: None reported		
Comparative			
Notes	Funding: Not stated Publication status: Published Paper Source: Revista da Associação Médica Brasileira Author COI: No COI statement reported		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		High risk	

Guclu 2020 (a) *(Continued)*

Are there concerns that the included patients and setting do not match the review question?

Low concern

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

Guclu 2020 (a) *(Continued)*

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Guclu 2020 (b)
Study characteristics

Patient Sampling	Two-group study (30 with and 19 without PCR-confirmed COVID infection) to estimate agreement between NP/OP and saliva samples for the diagnosis of COVID-19 Design: 49 (30) inpatients (day 3) with symptoms and CT findings compatible with COVID-19: [See Guclu 2020 (a) for report of single-group study of 15 symptomatic patients] Recruitment: Not stated Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Hospital inpatient Location: Sakarya University Training and Research Hospital Country: Turkey Dates: Not stated Symptoms and severity: CT findings consistent with COVID-19 and +ve PCR (complaints compatible with COVID-19 clinical symptoms, such as fever, cough, and shortness of breath, after examination by the head doctor) Demographics: Info provided for all 64 participants contributing to Guclu (a) and (b) combined: Mean age: 51 ± 17.9 years Male: 37/64 (57.8%) Exposure history: Not stated
Index tests	Reference Sample: Naso/oropharyngeal (NP/OP) Sample collected by: HCW Sample collection method: Dacron-flocked swab inserted first into the posterior oropharynx and the posterior pharynx was swabbed for 2-3 seconds. The swab was then inserted through the nostril with a rotation movement until the nasopharynx was reached and the sample was obtained by rotating the swab gently for 2-3 seconds. Swab then placed into a 5 mL tube containing 2 mL viral transport medium (VTM) Sample storage/transport: VTM; samples were delivered to the lab within one hour.

Guclu 2020 (b) *(Continued)*

Timing of sample collection: 3rd day of hospital admission
NAT extraction method: EZ1 (Qiagen, Germany) device

Assay used: genesis RT-PCR SARS-COV-2 (Primer Design, UK) kit

Genetic target: Not stated

Threshold: Ct value < 45

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva

Sample collection device: Not stated

Sample collected by: Supervised patient

Sample collection method: Patients were asked to collect the saliva sample themselves. They were given a sterile dry container and told to close the lid of the container after placing the saliva in it.

Sample storage/transport: Direct samples were delivered to the lab within one hour.

Timing of sample collection: 3rd day of hospital admission
NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Paired samples; second swab was taken to patients with a negative first sample.

Time interval between sampling methods: Simultaneously

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published Paper

Source: Revista da Associação Médica Brasileira

Author COI: No COI statement reported

Methodological quality

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Guclu 2020 (b) *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Guclu 2020 (b) (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Guzman-Ortiz 2021

Study characteristics

Patient Sampling	Design: [1] single group of paediatric participants who were COVID-19 non-confirmed or non-suspected patients [2] single group of paediatric participants confirmed positive for SARS-CoV-2 who were recovering at a COVID-19-specific area (preselected population of D+, not extracted for this review) [3] single group of adult participants members of the hospital staff from all departments (selective testing of NP/OP negatives, not extracted for this review) Recruitment: Unclear: '...the clinical criterion was the presence of at least one symptom related to SARS-CoV-2 infection. The exclusion criteria were: declined to participate and not provide enough saliva sample.' In figure 1, 73 exclusions were because 'no saliva sample was collected'. Prospective or retrospective: Prospective Sample size (cases): 156 (23) Additional inclusion criteria: Populations 2 and 3 excluded due to selected population (prior testing) and selected testing of NP/OP negatives.

Guzman-Ortiz 2021 (Continued)

Patient characteristics and setting

Setting: Hospital inpatient/outpatient
Location: Hospital Infantil de Mexico Federico Gomez
Country: Mexico
Dates: 4 May to 28 August 2020
Symptoms and severity: 91/156 (58.3%) symptomatic
128/156 ~ (82%) concurrent medical condition
Demographics: Age: Median (IQR): 11 years (7-14)
Sex: 78/156 (50%) male
Exposure history: Not stated

Index tests

Reference sample: Mixed NP/OP swabs

Sample collection device: Transport medium: Hanks' balanced salt solution without phenol red (Thermo Fisher Scientific, Waltham, MA, USA)

Sample collected by: Healthcare worker

Sample collection method: Not stated

Sample storage/transport: Hanks' balanced salt solution without phenol red (Thermo Fisher Scientific, Waltham, MA, USA). Specimens were kept at room temperature up to 4 h and then processed for viral RNA extraction or, if collected in late evening, kept at 4 °C overnight and processed the following morning.

Timing of sample collection: NS

NAT extraction method: QIAamp Viral RNA mini kit (QIAGEN, Hilden, Germany)

Assay used: GeneFinder COVID- 19 Plus RealAmp kit (ELITechGroup, Puteaux, France)

Genetic target: RdRp, E and N genes

Threshold: A sample was considered positive if at least one of the RdRp, N or E genes were amplified with a Ct ≤ 40.

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Where used, transport medium was Hanks' balanced salt solution without phenol red (Thermo Fisher Scientific, Waltham, MA, USA).

Sample collected by: patients/parents, no details provided

Sample collection method: Saliva was collected by the participants after being instructed to gently spit 5 times into a sterile 50 mL centrifuge tube; they were not instructed to cough out or try to enrich their samples with sputum.

Sample storage/transport: Dry/direct sampling or, where saliva was viscous, balanced salt solution without phenol red was added.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Guzman-Ortiz 2021 (Continued)

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 26 saliva specimens not tested: 6 saliva specimens not tested because of inadequate storage (5 days at 40 °C) and 20 samples with inadequate volume

Uninterpretable results: None reported

Indeterminate results: Test in saliva inconclusive 0

Comparative

Notes

Funding: CONACYT (PAACTI) and Federal funding from Hospital Infantil de Mexico Federico Gomez

Publication status: Published paper

Source: Frontiers in Pediatrics

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

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Guzman-Ortiz 2021 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type? No

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Yes

Could the conduct or interpretation of the index test have introduced bias? High risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, Yes

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Guzman-Ortiz 2021 *(Continued)*

different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)?

No

Were results presented per patient?

Yes

Were all patients included in the analysis?

No

Could the patient flow have introduced bias?

High risk

Hamilton 2021
Study characteristics

Patient Sampling

Design: Unclear group of paired nasopharyngeal (NP) swab and saliva specimens from symptomatic individuals during the months of August and September of 2020

Recruitment: Unclear

Prospective or retrospective: Retrospective

Sample size (cases): 128 (17)

Additional inclusion criteria: Info about NP tested by standard methods (ARUP NP assay) available; included RT-PCR or TMA testing

Patient characteristics and setting

Setting: Hospital outpatients

Location: Washington Hospital Healthcare System

Country: USA

Dates: August to September 2020

Symptoms and severity: All participants were symptomatic at testing time.

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal

Sample collection device: Not stated

Sample collected by: Healthcare worker

Sample collection method: Hospital's standard collection kit; no details provided

Sample storage/transport: IGI's swab sample collection medium (resulting in a 1:1 dilution). Within 2 hours, personnel at the WHHS clinical laboratory transferred 1 mL of swab-derived sample into the IGI's swab collection tube containing 1 mL 2x DNA/RNA Shield.

Timing of sample collection: NS

NAT extraction method: robotic sample plating and RNA extraction

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Hamilton 2021 (Continued)

Assay used: PCR method, no details provided

Genetic target: N gene

Threshold: Ct values < 38

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: OMNIgene OM-505 collection tubes (DNA Genotek)

Sample collected by: Supervised patient

Sample collection method: patients were guided through saliva sample collection using the OMNIgene saliva collection method.

Sample storage/transport: IGI's swab sample collection medium (resulting in a 1:1 dilution)

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference standard sample

Genetic target: As for reference standard sample

Threshold: As for reference standard sample

Blinding reported: As for reference standard sample

Threshold predefined: As for reference standard sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: 1 invalid data for the IGI NP assay, 5 for the IGI saliva assay

Indeterminate results: None reported

Comparative

Notes

Funding: Packard Foundation, the Curci Foundation and the Julia Burke Foundation to the Innovative Genomics Institute at UC Berkeley

Publication status: Published paper

Source: PLoS One

Author COI: J.A.D. is a cofounder of Caribou Biosciences, Editas Medicine, Scribe Therapeutics, Intellia Therapeutics and Mammoth Biosciences. J.A.D. is a scientific advisory board member of Caribou Biosciences, Intellia Therapeutics, eFFECTOR Therapeutics, Scribe Therapeutics, Mammoth Biosciences, Synthego, Algen Biotechnologies, Felix Biosciences and Inari. J.A.D. is a Director at Johnson & Johnson and has research projects sponsored by Biogen, Pfizer, AppleTree Partners and Roche. F.D.U. is a cofounder of Tune Therapeutics. P.G. is a cofounder and Director at NewCo Health. P.G. is the CLIA Laboratory Director for Coral Genomics and 3DMed. The other authors declared no competing interests.

Hamilton 2021 (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			

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DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Herrera 2021

Study characteristics

Patient Sampling	Design: Single group of consecutive asymptomatic healthcare and office workers Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 2107 (240) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Community Location: Mexico's National Cancer Institute and National Institute of Genomic Medicine Country: Mexico

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Herrera 2021 (Continued)

Dates: Not stated

Symptoms and severity: All subjects asymptomatic at enrolment

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swabs

Sample collection device: Single viral transport tube

Sample collected by: Healthcare worker (HCW)

Sample collection method: NP samples were collected using a flexible nylon swab that was inserted through the patient's nostrils to reach the posterior nasopharynx. It was left in place for several seconds and slowly removed while rotating.

Sample storage/transport: 3 mL of VTM. Sample collection was done within the same facilities where the viral diagnosis laboratory was located. Samples were processed for viral RNA extraction within 5 h after collection.

Timing of sample collection: Not stated

NAT extraction method: MagMAX Viral/Pathogen Nucleic Acid Isolation Kit (Thermo Fisher Scientific)

Assay used: US CDC realtime RT-qPCR protocol

Genetic target: N1 and N2 genes

Threshold: Ct value < 40

Blinding reported:

Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: 50 mL sterile conical centrifuge tube without preservatives

Sample collected by: Patients; no more details

Sample collection method: Saliva samples were self-collected by the individuals without any stimulation and without rinsing the mouth before sample collection.

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: As for reference standard

Assay used: As for reference standard

Genetic target: As for reference standard

Threshold: As for reference standard

Blinding reported: As for reference standard

Threshold predefined: As for reference standard

Herrera 2021 (Continued)

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 40 for NP swabs, 20 for saliva samples

Comparative

Notes

Funding: Secretaría de Educación, Ciencia, Tecnología e Innovación de la Ciudad de México (SECTEI)

Publication status: Published paper

Source: International Journal of Infectious Disease

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without	Unclear		

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Herrera 2021 (Continued)

knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias?

Unclear risk

Huber 2021 (a)

Study characteristics

Patient Sampling	Design: Single group of asymptomatic and symptomatic adults and children opting for a voluntary SARS-CoV-2 test with SARS-CoV-2-related symptoms based on Swiss testing criteria and asymptomatic individuals with relevant exposure to a SARS-CoV-2 index case at one of four dedicated outpatient testing centres or 1 AE department Could be subgrouped into [1] mixed [2] adults and [3] children Recruitment: Consecutive: 'Individuals were included without further selection to avoid skewing'. Prospective or retrospective: Prospective Sample size (cases): 1270 (273) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Dedicated outpatient test centres and emergency department Location: Institute of Medical Virology, University of Zurich, University Hospital Zurich, Spital Limmattal, Schlieren Staspital Triemli, Zurich, University Children's Hospital, Zurich Country: Switzerland Dates: From October 20, 2020 to 28th Jan 2021 Symptoms and severity: 960/1270 (75.6%) symptomatic Demographics: Age: median 34 (IQR 5-98) Sex: 693/1270 (54.6%) male Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: One tube with 3 mL VTM (Axonlab AL0607) Sample collected by: HCW-collected/laboratory staff-interpreted according to manufacturer's instructions Sample collection method: Saliva was collected directly after NPS. UTM or VTM swab, according to manufacturer's instructions Sample storage/transport: UTM or VTM: Cobas PCR Medium (Roche), Liquid amies preservation medium (Copan), Virus Preservative Medium (Improviral), or in-house VTM (HEPES, DMEM, FCS, antibiotics, antimycotics). Both specimens immediately sent for SARS-CoV-2 RT-PCR testing Timing of sample collection: Median 2 days (IQR 1-30) NAT extraction method: Nuclisens easyMAG Lysis Buffer (BioMérieux) Assay used: Threshold: Cobas SARS-CoV-2 IVD test (Roche) Genetic target: E and ORF1 Threshold: Ct values < 40 Blinding reported: NS Threshold predefined: Yes Index Sample: Saliva spit: 435/1270 (34%) enhanced spit (posterior oropharynx)

Huber 2021 (a) (Continued)

Sample collection device: One tube for saliva collection (Sarsted 105 62.555.001)

Sample collected by: Supervised patient-collected/laboratory staff-interpreted according to manufacturer's instructions

Sample collection method: Saliva was collected directly after NPS. VTM added to crude saliva.

Study arm - Basic: n = 835: individuals were asked to clear the throat thoroughly and collect saliva one or two times into the same tube.

Study arm - Enhanced: N = 435: clear their throat three times thoroughly and collect saliva into the same tube. Emphasis was put on throat clearing to ascertain sampling material from the posterior oropharynx.

Sample storage/transport: UTM or VTM

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: This work was supported by grants from the Swiss federal office of public health (FOPH) and the University of Zurich Foundation. Roche Diagnostics supported the study with PCR kits and consumables. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Publication status: Published paper

Source: Microorganisms

Author COI: No COI statement reported

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Yes

Huber 2021 (a) *(Continued)*

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	No
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	

Huber 2021 (a) (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Huber 2021 (b)

Study characteristics

Patient Sampling	Design: Single group of asymptomatic and symptomatic adults and children opting for a voluntary SARS-CoV-2 test with SARS-CoV-2-related symptoms based on Swiss testing criteria and asymptomatic individuals with relevant exposure to a SARS-CoV-2 index case at one of four dedicated outpatient testing centres or 1 AE department Could be subgrouped into [1] mixed [2] adults and [3] children Recruitment: Consecutive: 'Individuals were included without further selection to avoid skewing'. Prospective or retrospective: Prospective Sample size (cases): 1270 (273) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Dedicated outpatient test centres and emergency department

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Huber 2021 (b) (Continued)

Location: Institute of Medical Virology, University of Zurich, University Hospital Zurich; Spital Lim-mattal, Schlieren Staspital Triemli, Zurich;
University Children's Hospital, Zurich

Country: Switzerland

Dates: From October 20, 2020 to 28th Jan 2021

Symptoms and severity: 960/1270 (75.6%) symptomatic

Demographics: Age: median 34 (IQR 5-98)

Sex: 693/1270 (54.6%) male

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: One tube with 3 mL VTM (Axonlab AL0607)

Sample collected by: HCW-collected/laboratory staff-interpreted according to manufacturer's in-structions

Sample collection method: Saliva was collected directly after NPS.
UTM or VTM swab according to manufacturer's instructions.

Sample storage/transport: UTM or VTM: Cobas PCR Medium (Roche), Liquid amies preservation medium (Copan), Virus Preservative Medium (Improviral), or in-house VTM (HEPES, DMEM, FCS, an-tibiotics, antimycotics). Both specimens immediately sent for SARS-CoV-2 RT-PCR testing

Timing of sample collection: Median 2 days (IQR 1-30)

NAT extraction method: Nuclisens easyMAG Lysis Buffer (BioMérieux)

Assay used: Threshold: Cobas SARS-CoV-2 IVD test (Roche)

Genetic target: E and ORF1

Threshold: Ct values < 40

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit: 435/1270 (34%) enhanced spit (posterior oropharynx)

Sample collection device: One tube for saliva collection (Sarsted
105 62.555.001)

Sample collected by: Supervised patient-collected/laboratory staff-interpreted according to manu-facturer's instructions

Sample collection method: Saliva was collected directly after NPS.
VTM added to crude saliva

Study arm - Basic: n = 835: individuals were asked to clear the throat thoroughly and collect saliva one or two times into the same tube.

Study arm - Enhanced: N = 435: clear their throat three times thoroughly and collect saliva into the same tube. Emphasis was put on throat clearing to ascertain sampling material from the posterior oropharynx.

Sample storage/transport: UTM or VTM

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Huber 2021 (b) (Continued)

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: This work was supported by grants from the Swiss federal office of public health (FOPH) and the University of Zurich Foundation. Roche Diagnostics supported the study with PCR kits and consumables. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Publication status: Published paper

Source: Microorganisms

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and set-			Low concern

Huber 2021 (b) *(Continued)*

ting do not match the review
question?

DOMAIN 2: Index test (Saliva)

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

**Could the reference stan-
dard, its conduct, or its inter-
pretation have introduced
bias?**

**Are there concerns that the
target condition as defined
by the reference standard
does not match the ques-
tion?**

DOMAIN 4: Flow and timing

Was there an appropriate in-
terval between index tests? Yes

If multiple samples were taken
from individual patients (for
example on day 1 and day 2 af-
ter symptoms onset), did all
patients receive all index tests
(samples, different collection
methods) at each time point

Were the proportions and rea-
sons for missing data similar
across sample types (index
test)? Yes

Were results presented per pa-
tient? Yes

Were all patients included in
the analysis? Unclear

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Huber 2021 (b) (Continued)

Could the patient flow have introduced bias?

Unclear risk

Huber 2021 (c)

Study characteristics

Patient Sampling	Design: Single group of asymptomatic and symptomatic adults and children opting for a voluntary SARS-CoV-2 test with SARS-CoV-2-related symptoms based on Swiss testing criteria and asymptomatic individuals with relevant exposure to a SARS-CoV-2 index case at one of four dedicated outpatient testing centres or 1 AE department Could be subgrouped into [1] mixed [2] adults and [3] children Recruitment: Consecutive: 'Individuals were included without further selection to avoid skewing'. Prospective or retrospective: Prospective Sample size (cases): 1270 (273) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Dedicated outpatient test centres and emergency department Location: Institute of Medical Virology, University of Zurich, University Hospital Zurich; Spital Lim-mattal, Schlieren Staspital Triemli, Zurich; University Children's Hospital, Zurich Country: Switzerland Dates: From October 20, 2020 to 28th Jan 2021 Symptoms and severity: 960/1270 (75.6%) symptomatic Demographics: Age: median 34 (IQR 5-98) Sex: 693/1270 (54.6%) male Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: One tube with 3 mL VTM (Axonlab AL0607) Sample collected by: HCW-collected/laboratory staff-interpreted according to manufacturer's instructions Sample collection method: Saliva was collected directly after NPS. UTM or VTM swab according to manufacturer's instructions Sample storage/transport: UTM or VTM: Cobas PCR Medium (Roche), Liquid amies preservation medium (Copan), Virus Preservative Medium (Improviral), or in-house VTM (HEPES, DMEM, FCS, antibiotics, antimycotics). Both specimens immediately sent for SARS-CoV-2 RT-PCR testing. Timing of sample collection: Median 2 days (IQR 1-30) NAT extraction method: Nuclisens easyMAG Lysis Buffer (BioMérieux) Assay used: Threshold: Cobas SARS-CoV-2 IVD test (Roche) Genetic target: E and ORF1 Threshold: Ct values < 40

Huber 2021 (c) (Continued)

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit: 435/1270 (34%) enhanced spit (posterior oropharynx)

Sample collection device: One tube for saliva collection (Sarstedt 105 62.555.001)

Sample collected by: Supervised patient-collected/laboratory staff-interpreted according to manufacturer's instructions

Sample collection method: Saliva was collected directly after NPS.

VTM added to crude saliva

Study arm - Basic: n = 835: individuals were asked to clear the throat thoroughly and collect saliva one or two times into the same tube.

Study arm - Enhanced: N = 435: clear their throat three times thoroughly and collect saliva into the same tube. Emphasis was put on throat clearing to ascertain sampling material from the posterior oropharynx.

Sample storage/transport: UTM or VTM

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: This work was supported by grants from the Swiss federal office of public health (FOPH) and the University of Zurich Foundation. Roche Diagnostics supported the study with PCR kits and consumables. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Publication status: Published paper

Source: Microorganisms

Author COI: No COI statement reported

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

Huber 2021 (c) *(Continued)*
DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled? Yes

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Unclear

Did the study avoid inappropriate inclusions? Unclear

Was the intention that patients receive all tests at all time points? Yes

Could the selection of patients have introduced bias? Unclear risk

Are there concerns that the included patients and setting do not match the review question? Low concern

DOMAIN 2: Index test (Saliva)
DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

Huber 2021 (c) (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Justo 2021

Study characteristics

Patient Sampling	Design: Single group of São Paulo Hospital workers presenting with mild symptoms such as cough, fever, sore throat, rhinorrhoea, myalgia, headaches, insomnia, ageusia and fatigue Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 76 (41) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Other (HCW undergoing screening at their place of work) Location: Sao Paulo Hospital Country: Brazil Dates: October to December 2020 Symptoms and severity: 76/76 (100%) symptomatic Demographics: Mean age (range): 34.9 years (19-70) Sex: 23/76 (30.2%) male Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swabs

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Justo 2021 (Continued)

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Between 1 to 9 days pso

NAT extraction method: Quick-RNA Viral Kit (Zymo Research, Irvine, CA)

Assay used: multiplex RT-PCR commercial kit (GeneFinder, OSANG, South Korea)

Genetic target: RdRp, E and N genes

Threshold: A positive result was considered with a Ct value to lower than 40, for at least two SARS-CoV-2 genes (RdRp, E or N)

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva nos

Sample collection device: A sterile tube

Sample collected by: Patient/parent

Sample collection method: The subjects were asked to self-collect 2 mL of their saliva in a sterile tube, avoiding mucous secretions from the oropharynx and sputum.

Sample storage/transport: Dry/direct sampling

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: AFOJ and MSB are supported by grant 27968 (FUNDEP; FINEP, REDE COVID); GRB is supported by grant 2020/11719-0 (FAPESP); JMC is supported by CAPES.

Justo 2021 (Continued)

Publication status: Published paper

Source: Memórias do Instituto Oswaldo Cruz

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			

Justo 2021 (Continued)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Kannian 2021

Study characteristics

Patient Sampling	Design: Single group of patients with suspected COVID-19 symptoms recruited from the outpatient department and COVID-19 isolation wards Recruitment: Unclear, no information provided Prospective or retrospective: Retrospective Sample size (cases): 80 (57) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital (outpatient and inpatient) Location: VHS Hospital, Chennai

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Kannian 2021 (Continued)

Country: India

Dates: Not stated

Symptoms and severity: All patients symptomatic at testing
Information from COVID-19+ only in [Table 3](#):

16/55 (29%) mild disease

33/55 (60%) moderate disease

6/55 (11%) severe disease

Demographics: Information from COVID-19+ only in [Table 3](#):

34/55 (62%) male

17/55 (31%) between 20-40 years

21/55 (38%) between 41-60 years

17/55 (31%) ≥ 61 years

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swabs

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: swab, no details provided

Sample storage/transport: 3 mL of VTM. Samples were stored at 4 °C and processed within 24 h.

Timing of sample collection: NS

NAT extraction method: QIA Amp Viral RNA kit, Qiagen, Germany

Assay used: In-house RT-PCR using commercial mastermixes (Taq-man-based Labgenomics Labgun AssayPlus or Exofast, Siemens, Germany)

Genetic target: N and RdRp gene

Threshold: A cycle threshold (Ct) value of less than 37.5 with AssayPlus or 27.5 with Exofast for one or two of the genes was considered positive.

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva/whole mouth fluid

Sample collection device: Collected in sterile wide-mouthed screw-capped containers by drooling

Sample collected by: Not stated

Sample collection method: Not stated

Sample storage/transport: Direct. Samples were stored at 4 °C and processed within 24 h

Timing of sample collection: As for reference standard

NAT extraction method: As for reference standard

Assay used: As for reference standard

Genetic target: As for reference standard

Threshold: As for reference standard

Kannian 2021 (Continued)

Blinding reported: As for reference standard

Threshold predefined: As for reference standard

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Chennai Dental Research Foundation, Chennai, India

Publication status: Published paper

Source: Virus Research

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	No		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

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Kannian 2021 (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?

Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?

Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point

Yes

Were the proportions and reasons for missing data similar across sample types (index test)?

Unclear

Were results presented per patient?

Yes

Were all patients included in the analysis?

Unclear

Could the patient flow have introduced bias?

Unclear risk

Kerneis 2021 (a)

Study characteristics

Patient Sampling

Design: Single group of adults and children, either symptomatic or asymptomatic, referred to the two participating ambulatory community screening COV-ISAN centres in France

Recruitment: Consecutive

Prospective or retrospective: Prospective

Sample size (cases): 1328 (112)

Additional inclusion criteria:

Patient characteristics and setting

Setting: COVID-19 testing centres

Location: Assistance Publique-Hôpitaux de Paris, APHP

Country: France

Dates: 19 October to 18 December 2020

Symptoms and severity: 571/1451 (39%) were symptomatic on day of testing.

Demographics: Median age (IQR): 36 (26-50)

Sex: 696/1451 (48%) males

Exposure history: 564/1451 (39%) contact with a confirmed case

Index tests

Reference sample: Nasopharyngeal

Sample collection device: tubes containing 3 mL of transport medium with guanidium salt and nucleic acid stabiliser

Sample collected by: Healthcare worker

Sample collection method: Sterile nylon flocked swab

Sample storage/transport: UTM. Analysed within next 24 hours

Timing of sample collection: Median symptom onset 3 days (IQR 2-4)

NAT extraction method: MGIEasy Nucleic Acid Extraction Kit (MGI Tech Co, Shenzhen, China)

Assay used: TaqPath™ COVID 19 CE IVD RT PCR Kit (Thermo Fisher Scientific, Couteboeuf, France)

Genetic target: ORF1ab, N and S-genes

Threshold: NAAT results were considered positive if at least one gene was detected: either N, S, or ORF1ab (for MGI-1 and MGI-2), and either E or ORF1ab (for Roche).

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: 50 mL tube

Sample collected by: Supervised patient

Kerneis 2021 (a) (Continued)

Sample collection method: Participants were asked to salivate in their mouth without clearing their throat and to repeatedly spit into a 50 mL tube up to a maximum of 3 mL.

Sample storage/transport: Dry/direct sampling. Samples were frozen in several aliquots at -80 °C within 24 hours and stored for analysis.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Eight NPS (0.6%) and 24 saliva samples (1.7%) were not appropriately collected and were not analysed.

Uninterpretable results: Technical failure led to invalid results in 12 samples (none for nasopharyngeal NAAT, 8 for saliva MGI-2, and 4 for saliva Roche).

Indeterminate results: None reported

Comparative

Notes

Funding: French Ministry of Health and the Assistance Publique-Hôpitaux de Paris Foundation

Publication status: Published paper

Source: European Journal of Clinical Microbiology & Infectious Diseases

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		

Kerneis 2021 (a) *(Continued)*

Could the selection of patients have introduced bias?	Low risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	

Kerneis 2021 (a) (Continued)

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Unclear
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Kerneis 2021 (b)

Study characteristics

Patient Sampling	Design: Single group of adults and children, either symptomatic or asymptomatic, referred to the two participating ambulatory community screening COVISAN centres in France Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 1328 (112) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centres Location: Assistance Publique-Hôpitaux de Paris, APHP Country: France Dates: 19 October to 18 December 2020 Symptoms and severity: 571/1451 (39%) were symptomatic on day of testing. Demographics: Median age (IQR): 36 (26-50) Sex: 696/1451 (48%) males Exposure history: 564/1451 (39%) contact with a confirmed case
Index tests	Reference sample: Nasopharyngeal Sample collection device: tubes containing 3 mL of transport medium with guanidium salt and nucleic acid stabiliser Sample collected by: Healthcare worker Sample collection method: Sterile nylon flocked swab Sample storage/transport: UTM. Analysed within next 24 hours Timing of sample collection: Median symptom onset 3 days (IQR 2-4)

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Kerneis 2021 (b) (Continued)

NAT extraction method: MGIEasy Nucleic Acid Extraction Kit (MGI Tech Co, Shenzhen, China)

Assay used: TaqPath™ COVID 19 CE IVD RT PCR Kit (Thermo Fisher Scientific, Coutaboeuf, France)

Genetic target: ORF1ab, N and S-genes

Threshold: NAAT results were considered positive if at least one gene was detected: either N, S, or ORF1ab (for MGI-1 and MGI-2), and either E or ORF1ab (for Roche).

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: 50 mL tube

Sample collected by: Supervised patient

Sample collection method: Participants were asked to salivate in their mouth without clearing their throat and to repeatedly spit into a 50 mL tube up to a maximum of 3 mL.

Sample storage/transport: Dry/direct sampling. Samples were frozen in several aliquots at -80 °C within 24 hours and stored for analysis.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Eight NPS (0.6%) and 24 saliva samples (1.7%) were not appropriately collected and were not analysed.

Uninterpretable results: Technical failure led to invalid results in 12 samples (none for nasopharyngeal NAAT, 8 for saliva MGI-2, and 4 for saliva Roche).

Indeterminate results: None reported

Comparative

Notes

Funding: French Ministry of Health and the Assistance Publique-Hôpitaux de Paris Foundation

Publication status: Published paper

Source: European Journal of Clinical Microbiology & Infectious Diseases

Author COI: No COI statement reported

Kerneis 2021 (b) (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			
Are there concerns that the target condition as defined by the reference standard does not match the question?			
DOMAIN 4: Flow and timing			

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Kerneis 2021 (b) (Continued)

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms on-set), did all patients receive all index tests (samples, different collection methods) at each time point	Unclear
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Kerneis 2021 (c)

Study characteristics

Patient Sampling	Design: Single group of adults and children, either symptomatic or asymptomatic, referred to the two participating ambulatory community screening COVISAN centres in France Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 1328 (112): Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centres Location: Assistance Publique-Hôpitaux de Paris, APHP Country: France Dates: 19 October to 18 December 2020 Symptoms and severity: 571/1451 (39%) were symptomatic on day of testing. Demographics: Median age (IQR): 36 (26-50) Sex: 696/1451 (48%) males Exposure history: 564/1451 (39%) contact with a confirmed case
Index tests	Reference sample: Nasopharyngeal Sample collection device: tubes containing 3 mL of transport medium with guanidium salt and nucleic acid stabiliser Sample collected by: Healthcare worker

Kerneis 2021 (c) (Continued)

Sample collection method: Sterile nylon flocked swab

Sample storage/transport: UTM. Analysed within next 24 hours

Timing of sample collection: Median symptom onset 3 days (IQR 2-4)

NAT extraction method: MGIEasy Nucleic Acid Extraction Kit (MGI Tech Co, Shenzhen, China)

Assay used: TaqPath™ COVID 19 CE IVD RT PCR Kit (Thermo Fisher Scientific, Coutaboeuf, France)

Genetic target: ORF1ab, N and S-genes

Threshold: NAAT results were considered positive if at least one gene was detected: either N, S, or ORF1ab (for MGI-1 and MGI-2), and either E or ORF1ab (for Roche).

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: 50 mL tube

Sample collected by: Supervised patient

Sample collection method: Participants were asked to salivate in their mouth without clearing their throat and to repeatedly spit into a 50 mL tube up to a maximum of 3 mL.

Sample storage/transport: Dry/direct sampling. Samples were frozen in several aliquots at -80 °C within 24 hours and stored for analysis.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Eight NPS (0.6%) and 24 saliva samples (1.7%) were not appropriately collected and were not analysed.

Uninterpretable results: Technical failure led to invalid results in 12 samples (none for nasopharyngeal NAAT, 8 for saliva MGI-2, and 4 for saliva Roche).

Indeterminate results: None reported

Comparative

Notes

Funding: French Ministry of Health and the Assistance Publique-Hôpitaux de Paris Foundation

Publication status: Published paper

Kerneis 2021 (c) (Continued)

Source: European Journal of Clinical Microbiology & Infectious Diseases

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			
Are there concerns that the target condition as defined by the refer-			

Kerneis 2021 (c) (Continued)

ence standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Klein 2021

Study characteristics

Patient Sampling	Design: Single-group study Adults with symptoms suggestive of a SARS-CoV-2 infection or a recent high-risk contact with a confirmed SARS-CoV-2 case presented to a SARS-CoV-2 drive-in testing centre Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): Based on NPS RT-PCR: 290 (45) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Heidelberg (Division of Clinical Tropical Medicine, Centre of Infectious Diseases, Heidelberg University Hospital) Country: Germany Dates: December 15, 2020 to January 19, 2021 Symptoms and severity: 133/290 (45.9%) symptomatic Demographics: Age: Mean 42.7 (SD 14.6) years Sex: 138/290 (47.6%) male Exposure history: Not reported

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Klein 2021 (Continued)

Index tests

Reference sample: NPS

Sample collection device: Abbott Panbio (Rapid Diagnostics, Jane, Germany)

Sample collected by: HCW. Interpreted by trained study personnel following manufacturer's instructions

Order of collection and number of nostrils not clear

Sample collection method: flocked swab as part of commercial Ag kit (NFS-SWAB Applicator™, Noble Biosciences Inc., Gyeonggi-do, Korea)

Sample storage/transport. NA

Timing of sample collection: For symptomatic cases, mean 3.8 d (SD 5.4) pso

NAT extraction method: NA

Assay used: Panbio™ Ag-RDT (distributed by Abbott, Rapid Diagnostics, Jane, Germany)

Genetic target: Nucleocapsid antigen

Threshold: Commercial kit nos

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Nasal mid-turbinate

Sample collection device: As for reference sample

Sample collected by: Supervised patient/parent took swab. Interpreted by trained study personnel following manufacturer's instructions

Order of collection and number of nostrils not clear

Sample collection method: non-flocked swab (Jiangsu Changfeng Medical Industry Co., Ltd., Jiangsu, China) as part of the commercial RDT kit

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: One patient with invalid RT-PCR test result was excluded; one with lost written informed consent excluded

Uninterpretable results: One invalid AgRDT was registered on NP samples, which was valid upon repeat.

Klein 2021 (Continued)

Indeterminate results: 1 invalid RT-PCR test, the case excluded from the analysis

Comparative

Notes

Funding: Open Access funding enabled and organised by Projekt DEAL. The study was supported by Heidelberg University Hospital internal funds, as well as a grant from the Ministry of Science, Research and the Arts of Baden-Württemberg, Germany. The Foundation of Innovative New Diagnostics (FIND) reported grants from the UK Department of International Development (DFID, recently replaced by FCMO), grants from World Health Organization (WHO), and grants from Unitaid, to conduct the study.

Publication status: Published journal article

Source: Medical Microbiology and Immunology

Author COI: Authors declared no COIs.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		

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Klein 2021 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Kocagoz 2021

Study characteristics

Patient Sampling	Design: 363 volunteers above the age of 18, who were admitted to hospital with symptoms of respiratory infection Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 363 (114) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital inpatient Location: Acibadem Altunizade Hospital, Istanbul Country: Turkey Dates: Not stated Symptoms and severity: 363 (100%) symptomatic Demographics: Age: Not stated Sex: Not stated Exposure history: Not stated
Index tests	Reference sample: NPS Sample collection device: NS Sample collected by: HCW. Laboratory-interpreted Sample collection method: NS Sample storage/transport: NS Timing of sample collection: NS NAT extraction method: No extraction Assay used: Direct RT-PCR using commercial PCR kits (Bioeksen and A1 Lifesciences, Istanbul, Turkey) Genetic target: NS Threshold: Blinding reported: NS Threshold predefined: NS Index Sample: Unconcentrated mouthwash-gargle Sample collection device: NS Sample collected by: Patient. Laboratory-interpreted Sample collection method: After collecting nasopharyngeal swab samples, patients were instructed to take a few sips of regular drinking water, and then to gargle and rigorously rinse their mouth forcefully with this water for at least 10 s and put it back in an empty cup.

Kocagoz 2021 (Continued)

Sample storage/transport: NS

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: NS

Threshold predefined: NS

Target condition and reference standard(s)
Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative
Notes

Funding: None stated

Publication status: Published paper

Source: European Journal of Clinical Microbiology & Infectious Diseases

Author COI: The authors Tanil Kocagoz and Ozge Can are the founders of GigaBioMol and scientific advisors of Bio-T.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear

Kocagoz 2021 (Continued)

DOMAIN 2: Index test (Saliva)
DOMAIN 2: Index test (Gargle)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	No
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear

Could the conduct or interpretation of the index test have introduced bias? High risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Kocagoz 2021 (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Kojima 2020

Study characteristics

Patient Sampling	Two-group study to estimate agreement between HCW-collected NP swabs [Reference A]; HCW-supervised, patient-collected nasal swabs [Index A]; HCW-supervised, patient-collected saliva [Reference B & Index B] and unsupervised, patient-collected saliva [Index C] Design: 45 (29) non-hospitalised adults "recently" tested for COVID-19 as part of a drive-through testing programme. Recruitment: Participants who had recently attended drive-through COVID-19 testing were contacted by telephone or email to take part in the study. Response rate not provided Prospective or retrospective: Retrospective: "We aimed to recruit 30 persons that tested negative for COVID-19 and 30 persons that tested positive". Inclusion criteria: Adults older than 65 years, adults with chronic diseases, HCW and law enforcement officers exposed to COVID-19
Patient characteristics and setting	Setting: Community Location: University of California, Los Angeles Country: USA Dates: Not stated Symptoms and severity: 23/45 (51%) symptomatic Demographics: Median age: 42 years; IQR: 31 to 52 years Sex: Not stated Exposure history: Not stated
Index tests	Reference Sample [A] & [B]: Nasopharyngeal (NP) Sample collected by: HCW Sample collection method: Swab nos (Becton, Dickinson and Company, Franklin Lakes, NJ, USA) Sample storage/transport: Storage medium not stated. Samples were transported to the laboratory at ambient temperature for testing on the day of collection. Timing of sample collection: Cases: (29) ranged from 2-21 days of symptoms. Non-cases: (16) no details NAT extraction method: RNA purification kit, Norgen Biotek Corp, Thorold, ON, Canada

Kojima 2020 (Continued)

Assay used: RT-PCR single colour TaqMan probe modified by Integrated DNA Technologies, Coralville, IA, USA. Samples run on RT-PCR System (CFX 96™ Touch RT-PCR detection system or CFX 96™ Connect RT-PCR Detection System, Bio-Rad, Hercules, CA, USA)

Genetic target: N1, N2, N3. Ribonuclease P RNA served as a control.

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Unclear

Index Sample [A]: Nasal mid-turbinate

Sample collected by: Patient, supervised by a HCW

Sample collection method: Flocked swab (CLASSIQ Swabs, Copan Diagnostics, Murrieta, CA, USA). 'Insert swab into one nostril to depth 3-4 cm, rotate swab for 5-10 seconds (supposed mid-turbinate)

Sample storage/transport: Ribonucleic acid storage media (DNA/RNA Shield solution, Zymo Research Corp, Irvine, CA, USA)

Samples were transported to the laboratory at ambient temperature for testing on the day of collection.

Timing of sample collection: As for Reference sample

NAT extraction method: As for Reference sample

Assay used: As for Reference sample

Genetic target: As for Reference sample

Threshold: As for Reference sample

Blinding reported: Not stated

Threshold predefined: Unclear

Index Sample [B] & Reference Sample [C]: Saliva

Sample collected by: Patient, supervised by a HCW

Sample collection method: Sterile swab nos. Cough deeply 3-5 times, collect phlegm/secretions in mouth, rub swab on both cheeks, above and below tongue. Both gums and hard palate for 20 seconds

Sample storage/transport: As for Index sample A

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Unclear

Index Sample [C]: Saliva

Kojima 2020 (Continued)

Sample collected by: Patient

Sample collection method: Sterile swab nos. Cough deeply 3-5 times, collect phlegm/secretions in mouth, rub swab on both cheeks, above and below tongue. Both gums and hard palate for 20 seconds

Sample storage/transport: As for index sample A

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Unclear

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Not stated

Time interval between sampling methods: All samples collected within a 30-minute window

All patients received all sampling methods: Yes

Missing data: Authors reported one specimen as lost and the other two as having insufficient samples for laboratory analysis (3/180).

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: Pre-print (MedRxiv)

Author COI: Two authors declared having developed a COVID-19 viral assay for the detection of COVID-19 infection.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Unclear		

Kojima 2020 (Continued)

Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	High risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Unclear
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
If a threshold was used, was it pre-specified?	Unclear
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted	Unclear

Kojima 2020 (Continued)

without knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

If a threshold was used, was it pre-specified? Unclear

Is undergoing one sample type unlikely to influence the result of the other sample type? No

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias?

High risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

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Kojima 2020 (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Labhardt 2022

Study characteristics

Patient Sampling	Design: Single-group, 2-site study of adults and children presenting with symptoms compatible with COVID-19 and/or with a history of SARS-CoV-2 exposure meeting pre-defined screening criteria for testing: -body temperature $\geq 38^{\circ}\text{C}$ (non-contact forehead thermometer) or reporting at least one of 10 prespecified symptoms or contact with a probable or confirmed COVID-19 case in the last 14 days Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 1986 (115) Additional inclusion criteria: Only 2/3 sites performed all 3 tests. PCR results available for 2131 participants which was the population that the demographic information was presented for.
Patient characteristics and setting	Setting: Hospital outpatient Location: St Charles Missionary Hospital Seboch, Government District Hospital of Mokhotlong Country: Lesotho Dates: 28 Dec 2020-30 Sept 2021 Symptoms and severity: 1800/2131 (84.5%) symptomatic Demographics: Age: Median (IQR) 41 years (28-60) of 2131 Sex: 974/2131 (45.7%) male Exposure history: 78/2131 (3.6%) with known exposure to COVID-19 case
Index tests	Reference sample: NP swab Sample collection device: SD Biosensor STANDARD Q COVID-19 Ag Test kit Sample collected by: HCW-conducted and -interpreted Sample collection method: Nasopharyngeal sample collection was done after nasal sampling by inserting the nasopharyngeal swab in a horizontal position into the back of the nasopharynx until resistance was felt, while rotating the swab at least 5 times. Sample storage/transport: Within 15-30 minutes of sampling Commercial kit no further details Timing of sample collection: Mean duration of pso 4 days (2-7) (of 2131) NAT extraction method: NA

Labhardt 2022 (Continued)

Assay used: STANDARD Q COVID-19 Ag Test commercial test kits (SD Biosensor, Republic of Korea)

Genetic target: Nucleocapsid antigen

Threshold: Visible line considered as positive

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Nasal anterior nares swab

Sample collection device: As for reference sample

Sample collected by: As for reference sample

Sample collection method: Prior to sample collection, participants had to blow their nose. Once the participant was seated, with their head back slightly, the swab was inserted while rotating it in each nostril, gently pushing the swab up to about 2 cm into the nostril until resistance was met and rotated for 3-5 seconds.

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: NA

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 46/2198 NPS Ag and 88/2093 nasal ant Ag missing

Uninterpretable results: None reported

Indeterminate results: No Ag results reported as invalid

Comparative

Notes

Funding: Supported by Botnar Research Centre for Child Health (BRCH) as part of the Multi-Investigator Project/Fast Track Call for Acute Global Health Challenge
This work was also funded as part of FIND's work as co-convenor of the diagnostics pillar of the Access to COVID-19 Tools (ACT) Accelerator, including support from the government of the Netherlands and the World Health Organization.

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Labhardt 2022 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	No		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		

Labhardt 2022 (Continued)

Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	No
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk

Landry 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and saliva for the diagnosis of COVID-19 Design: 124 (35) symptomatic outpatients suspected of having COVID-19 attending a drive-through testing site Recruitment: April 16 to April 28, 2020

Landry 2020 (Continued)

	Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Hospital outpatient: drive-through testing site Location: Yale New Haven Hospital, Connecticut Country: USA Dates: April 16 to 28, 2020 Symptoms and severity: All patients were symptomatic; no further details provided Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: Not stated Sample collection method: Not stated Sample storage/transport: NPS stored in 3 mL of universal transport medium (Becton Dickinson), cooled and delivered for processing on the day of collection. Residual +ve NPS samples were frozen on day of receipt at -70 °C and thawed and tested 2 weeks later. Timing of sample collection: Not stated NAT extraction method: EasyMag (bioMerieux, Durham, NC) Assay used: RT-PCR LDT: developed assay based on the CDC protocol Genetic target: N1, N2 and RNase P Threshold: Not stated Blinding reported: Yes Threshold predefined: Probably yes (CDC protocol) Index Sample: Saliva Sample collected by: Patient Sample collection method: Patients were asked not to eat or drink for 30 min, let saliva pool in their mouths, and then spit into sterile containers. Sample storage/transport: Samples were kept in a cooler and delivered within 2 hours to the laboratory. Samples were frozen on the day of receipt at -70 °C and thawed and tested 2 weeks later. Viscous saliva samples were liquefied by treating with sputasol (Thermo Scientific). Timing of sample collection: Not stated NAT extraction method: As for Reference sample Assay used: RT-PCR LDT: As for Reference sample Genetic target: As for Reference sample Threshold: Not stated

Landry 2020 (Continued)

Blinding reported: Probably no; all NPS were tested on the day of collection. Only +ve NPS were subsequently stored for repeated testing at the same time as saliva samples.

Threshold predefined: Probably yes (CDC protocol)

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Probably yes

Time interval between sampling methods: Paired samples, probably within 24 hours of collection

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results

Comparative

Notes

Funding: No funding received

Publication status: Published Paper

Source: Journal of Clinical Virology

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Landry 2020 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	No
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes

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Landry 2020 (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Leung 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and saliva samples for the detection of SARS-CoV-2 Design: 95 (58) samples of 62 (29) patients admitted to hospital Recruitment: Unclear Prospective or retrospective: Retrospective
Patient characteristics and setting	Setting: Hospital inpatient Location: Prince of Wales Hospital, Hong Kong Country: China Dates: February-March 2020 Symptoms and severity: Not stated Demographics: Mean age: 42 ± 17.1 years; range from 19 to 85 years Sex: 26/62 (41%) male Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: HCW (nursing staff) Sample collection method: Swab: flocked swabs Sample storage/transport: VTM (3 mL) in a container (no further details provided) Collected specimens were sent to a laboratory immediately for testing. Timing of sample collection: Not stated NAT extraction method: Viral RNA isolation kit (Applied Biosystem, Foster City) + MagMAX kit Assay used: LightMix Modular SARS-CoV (COVID-19) E-gene detection kit (TIB Molbiol, Berlin, Germany). Test positive received additional different RT PCR assay(s) (nos) Genetic target: E gene and RdRp gene Threshold: E gene and RdRp gene both positive. No further detail Blinding reported: Not stated Threshold predefined: Yes Index Sample: Saliva

Leung 2020 (Continued)

Sample collected by: Patient

Sample collection method: Patients were provided with clear instructions to collect saliva from the deep throat (posterior oropharynx).

Sample storage/transport: VTM (2 mL) collected in a 'sterile sputum container'. Collected specimens were sent to a laboratory immediately for testing.

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Samples collected the same day

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published paper

Source: Academic journal

Author COI: Authors declared no COI.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Was a case-control design avoided?

Yes

Did the study avoid inappropriate exclusions?

Unclear

Did the study avoid inappropriate inclusions?

Unclear

Leung 2020 (Continued)

Was the intention that patients receive all tests at all time points? Unclear

Could the selection of patients have introduced bias? Unclear risk

Are there concerns that the included patients and setting do not match the review question? Unclear

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing
The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Leung 2020 (Continued)

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	No
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Lindner 2021

Study characteristics

Patient Sampling	Design: Single-group study Symptomatic adults with high clinical suspicion of SARS-CoV-2 including 1) reported contact with a confirmed case and any compatible symptom, or 2) fever or impaired taste or smell irrespective of exposure Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 146 (40) Additional inclusion criteria: Only participants who were able to understand the written instructions in English or German were included (required to fulfill the CEFR language criterion) Participants were excluded if any of the swabs could not be collected.
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Ambulatory SARS-CoV-2 testing facility of Charité University Hospital, Berlin Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health; Institute of Tropical Medicine and International Health, Berlin Country: Germany Dates: 30 Nov-11 Dec 2020 Symptoms and severity: 100% symptomatic; mean duration of pso 3.4 days (SD 2.0) 34 (23%) with comorbidities Demographics: Mean age 35 years (SD 11.5); 75 (51%) were female Exposure history: Included those with reported contact with a confirmed case. No further details on 'n'
Index tests	Reference sample: Nasopharyngeal swab Sample collection device: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Lindner 2021 (Continued)

Sample collected by: Trained HCW-collected/trained HCW-interpreted according to manufacturer's instructions

Sample collection method: Flexible flocked NP swab after NMT swab collection

Interpretation: Professional test interpretation was by two study physicians, each blinded to the result of the other

Sample storage/transport: Commercial kit nos

Timing of sample collection: Mean duration of pso 3.4 days (SD 2.0)

NAT extraction method: NA

Assay used: Ag (CGIA)

Standard Q COVID-19 Ag Test

SD Biosensor, Inc. Gyeonggi-do, Korea; also distributed by Roche

Genetic target: Nucleocapsid antigen

Threshold: The visual read-out of the antigen test band was categorised as negative, weak positive, positive, or strong positive.

Weak positives were classified as positive.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Nasal mid-turbinate: Self-collection and self-testing (interpretation)

Sample collection device: Not stated

Sample collected by: Unsupervised patient-collected/unsupervised patient-interpreted according to manufacturer's instructions

Sample collection method: Collection:

Flocked swab. 'Nasal swabs used for self-sampling less flexible with a larger sampling surface compared to NP swabs'. Mirror and timer provided. Observed by HCW but no intervention.

1) "Cover your nose with a tissue and blow once"; 2) "Remove the swabs from the packaging" ... 3) "Tilt your head back slightly (angle approx. 70 degrees)"; 4) "Insert the swab into a nostril with the cotton swab first. Slowly move the swab forward about 2 cm according to the angle (parallel to the palate = towards the throat, not upwards) until you feel resistance, do not apply pressure"; 5) "Slowly rotate the swab around for 15 seconds (minimum 4 rotations), rubbing all sides of the swab against the inside of the nose"; 6) "Repeat the procedure with the same swab in the other nostril".

Interpretation: After 15 minutes, the participant was asked to state his/her interpretation of the test result (positive, negative, invalid, or don't know).

'The participants received written and illustrated instructions in German or English, adapted from the manufacturer's instructions for use'.

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAT extraction method: NA

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Lindner 2021 (Continued)

Threshold predefined: As for reference sample

Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: Index and index reference samples: 4 excluded (3 participants were excluded as they did not fulfil the minimum language criterion 1 participant excluded because of lost PCR specimen) Uninterpretable results: Nasal MT: N = 2 One participant left without reading the test result for nasal sample plus one invalid result (buffer spilt and test not repeated); Indeterminate results: None reported
Comparative	
Notes	Funding: The study was supported by Foundation of Innovative New Diagnostics (FIND), Charité University Hospital internal funds, as well as a grant from the Ministry of Science, Research and the Arts of Baden-Württemberg, Germany. Publication status: Published paper Source: Journal of Clinical Virology Author COI: One author reported grants from FIND and Ministry of Science, Research and Culture, State of Baden Wuerttemberg, Germany. Another author reported grants from DFID (recently replaced by FCMO), WHO and from Unitaid.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Lindner 2021 (Continued)

DOMAIN 2: Index test (Saliva)
DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Yes

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Yes

Could the conduct or interpretation of the index test have introduced bias? Low risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

Lindner 2021 (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Lopes 2021
Study characteristics

Patient Sampling	Design: Two single-group cohorts of patients: Admitted consecutively to Haematology inpatient ward or healthcare workers with suspected COVID-19 or in close contact with people who tested positive for COVID-19 Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): NP vs OP: 1440 (267) NP vs saliva: 1440 (295) NP vs saliva VTM: 1440 (280) Additional inclusion criteria: No 2 x 2 tables reported, calculations made based on the numbers reported on page 6; estimated sens/spec were slightly different to those reported in Table 1
Patient characteristics and setting	Setting: Mixed: Hospital inpatient + HCW Location: Instituto de Hematologia Arthur de Siqueira Cavalcanti/Hemorio Country: Brazil Dates: January 2020 to April 2021 Symptoms and severity: 645/1683 (38.3%) symptomatic Demographics: Age: Mean (SD): 35.59 (21.82) Sex: 690/1683 (41%) male

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Lopes 2021 (Continued)

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: 5 mL tube

Sample collected by: Healthcare workers

Sample collection method: NPS collection was performed by rubbing a swab on the posterior part of the nostril, with a rotation movement until the nasopharynx was reached, and the sample was obtained by rotating the swab gently for 5 s.

Sample storage/transport: 3 mL viral transport medium (VTM). Samples stored at -80 °C until RNA extraction. Samples were immediately transported to the laboratory; no other details provided

Timing of sample collection: NS

NAT extraction method: Automatic MDX Biorobot® (Qiagen, Hilden, Germany)

Assay used Molecular kit SARS-CoV-2 (E) (Bio-Manguinhos/Fiocruz, Rio de Janeiro, Brazil)

Genetic target: RdRp and E genes

Threshold: Ct-values < 40 were considered positive.

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Oropharyngeal swab

Sample collection device: 5 mL tube

Sample collected by: Healthcare workers

Sample collection method: For the collection of the OPS, the swab was inserted in the oral cavity, then rubbed on the posterior part of the pharynx and regions of the tonsils, avoiding contact with the tongue, teeth, and gums.

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Index Sample (B): Saliva spit (VTM)

Sample collection device: Sterile sputum containers containing 300 uL of 0.9% NaCl solution

Sample collected by: Supervised patient

Sample collection method: Patients were requested to avoid eating, drinking, and smoking for at least 30 min prior to spitting into the sterile tube containing saline

Lopes 2021 (Continued)

solution (0.9% NaCl). Specimens were considered acceptable if at least 1 mL of saliva had been obtained.

Sample storage/transport: Saline solution. An aliquot of 300 uL of saliva was transferred to sterile tubes and mixed with 300 uL of VTM. Samples stored at -80 °C until RNA extraction. Samples were immediately transported to the laboratory; no other details provided

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: 1629 NP samples, 1498 saliva samples and 1596 OP samples reported; no reasons for missing samples provided

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Oswaldo Cruz Institute (IOC-FIOCRUZ)

Publication status: Published paper

Source: Viruses

Author COI: Authors declared no COI present.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Yes

Was a case-control design avoided?

Yes

Did the study avoid inappropriate exclusions?

Unclear

Did the study avoid inappropriate inclusions?

Unclear

Was the intention that patients receive all tests at all time points?

Unclear

Lopes 2021 (Continued)

Could the selection of patients have introduced bias?

Unclear risk

Are there concerns that the included patients and setting do not match the review question?

Low concern

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias?

Low risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias?

Low risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

Lopes 2021 (Continued)

DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point No

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Unclear

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Mahmoud 2021
Study characteristics

Patient Sampling	Design: Unclear
	Recruitment: Unclear
	Prospective or retrospective: Prospective
	Sample size (cases): 595 (250)
	Additional inclusion criteria: 5 invalid samples excluded for main analysis; additional information for a subsample of participants (n = 231) using an alternative PCR kit and comparing the two commercial kits used (n = 254)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Mahmoud 2021 (Continued)

Patient characteristics and setting

Setting: Unclear

Location: G42 Healthcare Biogenix Laboratory

Country: United Arab Emirates

Dates: Not stated

Symptoms and severity: Not stated

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal

Sample collection device: Not stated

Sample collected by: Healthcare worker

Sample collection method: Not stated

Sample storage/transport: Viral transport medium

Timing of sample collection: Not stated

NAT extraction method: "RNA extraction was performed by the automated machine MGISP-960, as per the manufacturer's instructions".

Assay used: BGI Genomics' 2019-nCoV Fluorescence Detection Real-Time RT-PCR kit

Genetic target: ORF1ab

Threshold: Threshold predefined: Ct values < 38

Blinding reported: Yes

Index Sample: Saliva spit

Sample collection device: sterile Dnase/Rnase-free container

Sample collected by: Patient; no details provided

Sample collection method: Participants were asked to pool saliva in his or her mouth for 1–2 minutes before depositing the salivary sample into a collection tube.

Sample storage/transport: Dry/direct sampling. Salivary samples were transported to the lab in temperature-controlled boxes at 2–8 degrees Celsius.

Timing of sample collection: Not stated

NAT extraction method: No RNA extraction

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Mahmoud 2021 (Continued)

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: 5 invalid samples for the main analysis

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published paper

Source: Biomed Research International

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		

Mahmoud 2021 (Continued)

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias?

Unclear risk

Marquette 2021 (a)

Study characteristics

Marquette 2021 (a) (Continued)

Patient Sampling	Design: [1] Mix of symptomatic subjects referred by their attending physician because of recent (≤ 2 weeks) symptoms of COVID-19 and close contacts: subjects referred by the contact tracing staff of the French public health insurance [2] Symptomatics: subjects referred by their attending physician because of recent (≤ 2 weeks) symptoms of COVID-19 [3] Close contacts: subjects referred by the contact tracing staff of the French public health insurance Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): [1] 409 (116) [2] 147 (59) [3] 262 (57) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Nice-Côte d'Azur Metropolis community-based COVID-19 centre, Nice Country: France Dates: [1] Sept 21, 2020 to March 8, 2021 [2] Sept 21, 2020 to Jan 6, 2021 [3] Feb 6 to March 8, 2021 Symptoms and severity: [a] NS [b] 147/147 (100%) symptomatic [c] NS Demographics: [a] Age: NS Sex: 178/409 (44%) male [b] Age: Mean 40 (SD ± 15 years) Sex: 61/147 (42%) male [c] Age: Mean 41 (SD ± 15 years) Sex: 117/262 (45%) male Exposure history: [a] NS [b] NS [c] 262/262 (100%) with known exposure to COVID-19 case
Index tests	Reference sample: NP swab Sample collection device: Disposable NP nylon swabs (type A-04. Jiangsu Han-Heng Medical technology Co., Ltd. Changzhou, Jiangsu, China) Sample collected by: Patient/parent Sample collection method: Samples were eluted into a vial. 'After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: NP and OS in a random order'. Sample storage/transport: Viral transport medium. Transported within 4 hours

Marquette 2021 (a) (Continued)

Timing of sample collection: If symptomatic: 3.6 ± 2.6 days (mean $\pm$ SD)

NAT extraction method: Symptomatics: Viral RNA extraction buffer (RNA/DNA purification kit, DaAn Gene, ref DA0940)

Close contacts: no RNA extraction (TMA technique)

Assay used: Symptomatics: DaAnGene DA0992-Detection Kit for 2019-nCoV (DaAn Gene Co., Ltd. Sun Yat-sen University, Guangzhou, Guangdong, China)

Close contacts: Aptima SARS-CoV-2 assay (Hologic, Inc. 10210 Genetic Center Drive San Diego, CA 92121, USA)

Genetic target: Symptomatics: N, ORF1ab gene

Close contacts: ORF1ab gene

Threshold: Symptomatics: Ct < 36 for positivity

Close contacts: RLU above 850

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Small hydroxylated polyvinyl acetate (PVA) sponges (Merocel® Standard Dressing, réf 400400, Medtronic)

Sample collected by: NS, assume HCW

Sample collection method: Small hydroxylated poly vinyl acetate (PVA) sponges placed in mouth by subjects and taken out after one minute and inserted into a sterile collection tube

No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette.

'After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: NP and OS in a random order'.

Sample storage/transport: Medium not stated. Transported within 4 hours

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference standard

Threshold: As for reference standard

Blinding reported: As for reference standard

Threshold predefined: As for reference

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by Conseil Départemental 06, Ville de Nice, Métropole Nice Côte d'Azur, Fonds de Dotation AVENI, and from private donors

Marquette 2021 (a) (Continued)

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Marquette 2021 (a) *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias?

Low risk

Marquette 2021 (b)

Study characteristics

Patient Sampling	Design: [1] Mix of symptomatic subjects referred by their attending physician because of recent (≤ 2 weeks) symptoms of COVID-19 and close contacts: subjects referred by the contact tracing staff of the French public health insurance [2] Symptomatics: subjects referred by their attending physician because of recent (≤ 2 weeks) symptoms of COVID-19 [3] Close contacts: subjects referred by the contact tracing staff of the French public health insurance Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): [1] 409 (116) [2] 147 (59) [3] 262 (57) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Nice-Côte d'Azur Metropolis community-based COVID-19 centre, Nice Country: France Dates: [1] Sept 21 2020 to March 8, 2021 [2] Sept 21, 2020 to Jan 6, 2021 [3] Feb 6 to March 8, 2021 Symptoms and severity: [a] NS [b] 147/147 (100%) symptomatic [c] NS Demographics: [a] Age: NS Sex: 178/409 (44%) male [b] Age: Mean 40 (SD ± 15 years) Sex: 61/147 (42%) male [c] Age: Mean 41 (SD ± 15 years) Sex: 117/262 (45%) male Exposure history: [a] NS [b] NS [c] 262/262 (100%) with known exposure to COVID-19 case

Index tests	Reference sample: NP swab Sample collection device: Disposable NP nylon swabs (type A-04. Jiangsu Han-Heng Medical technology Co., Ltd. Changzou, Jiangsu, China) Sample collected by: patient/parent Sample collection method: Samples were eluted into a vial.

Marquette 2021 (b) (Continued)

'After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: NP and OS in a random order'.

Sample storage/transport: Viral transport medium. Transported within 4 hours

Timing of sample collection: If symptomatic: 3.6 ± 2.6 days (mean $\pm$ SD)

NAT extraction method: Symptomatics: Viral RNA extraction buffer (RNA/DNA purification kit, DaAn Gene, ref DA0940)

Close contacts: no RNA extraction (TMA technique)

Assay used: Symptomatics: DaAnGene DA0992-Detection Kit for 2019-nCoV (DaAn Gene Co., Ltd. Sun Yat-sen University, Guangzhou, Guangdong, China)

Close contacts: Aptima SARS-CoV-2 assay (Hologic, Inc. 10210 Genetic Center Drive San Diego, CA 92121 USA)

Genetic target: Symptomatics: N, ORF1ab gene

Close contacts: ORF1ab gene

Threshold: Symptomatics: Ct < 36 for positivity

Close contacts: RLU above 850

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Small hydroxylated polyvinyl acetate (PVA) sponges (Merocel® Standard Dressing, réf 400400, Medtronic)

Sample collected by: NS, assume HCW

Sample collection method: small hydroxylated poly vinyl acetate (PVA) sponges placed in mouth by subjects and taken out after one minute and inserted into a sterile collection tube

No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette.

'After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: NP and OS in a random order'.

Sample storage/transport: Medium not stated. Transported within 4 hours

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference standard

Threshold: As for reference standard

Blinding reported: As for reference standard

Threshold predefined: As for reference

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Marquette 2021 (b) (Continued)

Notes

Funding: Supported by Conseil Départemental 06, Ville de Nice, Métropole Nice Côte d'Azur, Fonds de Dotation AVENI, and from private donors

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			

Marquette 2021 (b) (Continued)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Low risk

Marquette 2021 (c)

Study characteristics

Patient Sampling	Design: [1] Mix of symptomatic subjects referred by their attending physician because of recent (≤ 2 weeks) symptoms of COVID-19 and close contacts: subjects referred by the contact tracing staff of the French public health insurance [2] Symptomatics: subjects referred by their attending physician because of recent (≤ 2 weeks) symptoms of COVID-19 [3] Close contacts: subjects referred by the contact tracing staff of the French public health insurance Recruitment: Consecutive Prospective or retrospective: Prospective

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Marquette 2021 (c) (Continued)

Sample size (cases):

[1] 409 (116)

[2] 147 (59)

[3] 262 (57)

Additional inclusion criteria: None

Patient characteristics and setting

Setting: COVID-19 testing centre/drive-through

Location: Nice-Côte d'Azur Metropolis community-based COVID-19 centre, Nice

Country: France

Dates:

[1] Sept 21 2020 to March 8, 2021

[2] Sept 21, 2020 to Jan 6, 2021

[3] Feb 6 to March 8, 2021

Symptoms and severity:

[a] NS

[b] 147/147 (100%) symptomatic

[c] NS

Demographics:

[a]

Age: NS

Sex: 178/409 (44%) male

[b]

Age: Mean 40 (SD $\pm$ 15 years)

Sex: 61/147 (42%) male

[c]

Age: Mean 41 (SD $\pm$ 15 years)

Sex: 117/262 (45%) male

Exposure history:

[a] NS

[b] NS

[c] 262/262 (100%) with known exposure to COVID-19 case

Index tests
Reference sample: NP swab

Sample collection device: Disposable NP nylon swabs (type A-04. Jiangsu Han-Heng Medical technology Co., Ltd. Changzou, Jiangsu, China)

Sample collected by: Patient/parent

Sample collection method: Samples were eluted into a vial.

'After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: NP and OS in a random order'.

Sample storage/transport: Viral transport medium. Transported within 4 hours

Timing of sample collection: If symptomatic: 3.6 ± 2.6 days (mean $\pm$ SD)

NAT extraction method: Symptomatics: Viral RNA extraction buffer (RNA/DNA purification kit, DaAn Gene, ref DA0940)

Close contacts: no RNA extraction (TMA technique)

Assay used: Symptomatics: DaAnGene DA0992-Detection Kit for 2019-nCoV (DaAn Gene Co., Ltd. Sun Yat-sen University, Guangzhou, Guangdong, China)

Close contacts: Aptima SARS-CoV-2 assay (Hologic, Inc. 10210 Genetic Center Drive San Diego, CA 92121 USA)

Genetic target: Symptomatics: N, ORF1ab gene

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Marquette 2021 (c) (Continued)

Close contacts: ORF1ab gene

Threshold: Symptomatics: Ct < 36 for positivity

Close contacts: RLU above 850

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Small hydroxylated polyvinyl acetate (PVA) sponges (Merocel® Standard Dressing, réf 400400, Medtronic)

Sample collected by: NS, assume HCW

Sample collection method: Small hydroxylated poly vinyl acetate (PVA) sponges placed in mouth by subjects and taken out after one minute and inserted into a sterile collection tube

No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette.

'After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: NP and OS in a random order'.

Sample storage/transport: Medium not stated. Transported within 4 hours

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference standard

Threshold: As for reference standard

Blinding reported: As for reference standard

Threshold predefined: As for reference

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by Conseil Départemental 06, Ville de Nice, Métropole Nice Côte d'Azur, Fonds de Dotation AVENI, and from private donors

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Marquette 2021 (c) *(Continued)*

Was a consecutive or random sample of patients enrolled? Yes

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Did the study avoid inappropriate inclusions? Yes

Was the intention that patients receive all tests at all time points? Yes

Could the selection of patients have introduced bias? Low risk

Are there concerns that the included patients and setting do not match the review question? Low concern

DOMAIN 2: Index test (Saliva)

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

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Marquette 2021 (c) *(Continued)*

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Low risk

Marx 2021 (a)
Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled during community testing at homeless service sites and dedicated COVID-19 testing clinics (n = 730) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal ant: 70/563 (12%) Saliva: 60/496 (12%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed community (homeless and dedicated COVID-19 testing sites) Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 269/730 (36.8%) Demographics: 420/730 (57.5%) male; median age 43 Exposure history: 159/730 (21.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab

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Marx 2021 (a) (Continued)

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated VTM.

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay
Genetic target: N1, N2 gene

Threshold: Ct < 40 for positivity

Blinding reported:

Threshold predefined: Yes

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines)

Sample storage/transport: Not stated; CDC Guideline stated no VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 3%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Marx 2021 (a) (Continued)

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

Marx 2021 (a) (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (b)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled during community testing at homeless service sites and dedicated COVID-19 testing clinics (n = 730) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal ant: 70/563 (12%) Saliva: 60/496 (12%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed community (homeless and dedicated COVID-19 testing sites)

Marx 2021 (b) (Continued)

Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia)

Country: USA and Georgia

Dates: August-November 2020

Symptoms and severity: 269/730 (36.8%)

Demographics: 420/730 (57.5%) male; median age 43

Exposure history: 159/730 (21.8%) known exposure within 2 weeks

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated VTM.

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene

Threshold: Ct < 40 for positivity

Blinding reported:

Threshold predefined: Yes

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated no VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

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Marx 2021 (b) (Continued)

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b].

Uninterpretable results: Insufficient saliva 3%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			

Marx 2021 (b) (Continued)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (c)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled during community testing at homeless service sites and dedicated COVID-19 testing clinics (n = 730) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal ant: 70/563 (12%) Saliva: 60/496 (12%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed community (homeless and dedicated COVID-19 testing sites) Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia

Marx 2021 (c) (Continued)

Dates: August-November 2020

Symptoms and severity: 269/730 (36.8%)

Demographics: 420/730 (57.5%) male; median age 43

Exposure history: 159/730 (21.8%) known exposure within 2 weeks

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated VTM.

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene

Threshold: Ct < 40 for positivity

Blinding reported:

Threshold predefined: Yes

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated no VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b].

Uninterpretable results: Insufficient saliva 3%

Marx 2021 (c) (Continued)

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			

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Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (d)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled during community testing at homeless service sites and dedicated COVID-19 testing clinics (n = 730) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal ant: 70/563 (12%) Saliva: 60/496 (12%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed community (homeless and dedicated COVID-19 testing sites) Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 269/730 (36.8%)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Marx 2021 (d) (Continued)

Demographics: 420/730 (57.5%) male; median age 43
Exposure history: 159/730 (21.8%) known exposure within 2 weeks

Index tests

Reference sample: NP swab

Sample collection device: Not stated
Sample collected by: HCW-collected/HCW-interpreted
Sample collection method: Not stated (specimens were collected according to current CDC guidelines).
Sample storage/transport: Not stated; CDC Guideline stated VTM.
Timing of sample collection: Not stated
NAT extraction method: Not stated
Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay
Genetic target: N1, N2 gene
Threshold: Ct < 40 for positivity
Blinding reported:
Threshold predefined: Yes

Index Sample (B): Nasal anterior nares swab

Sample collection device: Not stated
Sample collected by: Supervised patient collection/HCW-interpreted
Sample collection method: Not stated (specimens were collected according to current CDC guidelines).
Sample storage/transport: Not stated; CDC Guideline stated VTM.
Timing of sample collection: As for reference sample
NAT extraction method: As for reference sample
Assay used: As for reference sample
Genetic target: As for reference sample
Threshold: As for reference sample
Blinding reported: As for reference sample
Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes
Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b].
Uninterpretable results: Insufficient saliva 3%
Indeterminate results: None reported

Comparative

Marx 2021 (d) (Continued)

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without	Unclear		

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (d) (Continued)

knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias?

High risk

Marx 2021 (e)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled during community testing at homeless service sites and dedicated COVID-19 testing clinics (n = 730)
	Recruitment: Unclear
	Prospective or retrospective: Unclear. Probably prospective
	Sample size (cases): Nasal ant: 70/563 (12%) Saliva: 60/496 (12%)
	Additional inclusion criteria: None

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Marx 2021 (e) (Continued)

Patient characteristics and setting	Setting: Mixed community (homeless and dedicated COVID-19 testing sites) Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 269/730 (36.8%) Demographics: 420/730 (57.5%) male; median age 43 Exposure history: 159/730 (21.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated; CDC Guideline stated VTM. Timing of sample collection: Not stated NAT extraction method: Not stated Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity Blinding reported: Threshold predefined: Yes Index Sample (B): Nasal anterior nares swab Sample collection device: Not stated Sample collected by: Supervised patient collection/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated; CDC Guideline stated VTM. Timing of sample collection: As for reference sample NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample

Marx 2021 (e) (Continued)

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 3%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (e) (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Marx 2021 (f)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled during community testing at homeless service sites and dedicated COVID-19 testing clinics (n = 730)
	Recruitment: Unclear
	Prospective or retrospective: Unclear. Probably prospective
	Sample size (cases): Nasal ant: 70/563 (12%) Saliva: 60/496 (12%)
	Additional inclusion criteria: None

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (f) (Continued)

Patient characteristics and setting	Setting: Mixed community (homeless and dedicated COVID-19 testing sites) Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 269/730 (36.8%) Demographics: 420/730 (57.5%) male; median age 43 Exposure history: 159/730 (21.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated; CDC Guideline stated VTM. Timing of sample collection: Not stated NAT extraction method: Not stated Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity Blinding reported: Threshold predefined: Yes Index Sample (B): Nasal anterior nares swab Sample collection device: Not stated Sample collected by: Supervised patient collection/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated; CDC Guideline stated VTM. Timing of sample collection: As for reference sample NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample

Marx 2021 (f) (Continued)

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 3%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (f) (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Marx 2021 (g)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled at clinical settings at a large public hospital (n = 1076)
	Recruitment: Unclear
	Prospective or retrospective: Unclear. Probably prospective
	Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%)
	Additional inclusion criteria: None

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (g) (Continued)

Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 610/1076 (56.7%) Demographics: 559/1076 (52%) male; median age 52 Exposure history: 30/1076 (2.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated. CDC Guideline stated VTM. Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic NAT extraction method: Not stated Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity Blinding reported: NS Threshold predefined: Yes Index Sample (A): Saliva swab Sample collection device: Not stated Sample collected by: Supervised patient collection/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated; CDC Guideline stated bo VTM. Timing of sample collection: As for reference sample NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (g) (Continued)

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Marx 2021 (g) (Continued)

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (h)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076)
	Recruitment: Unclear
	Prospective or retrospective: Unclear. Probably prospective

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (h) (Continued)

Sample size (cases): Nasal: 74/932 (8%)

Saliva: 69/864 (8%)

Additional inclusion criteria: None

Patient characteristics and setting

Setting: Mixed hospital (A&E and 'other')

Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia)

Country: USA and Georgia

Dates: August-November 2020

Symptoms and severity: 610/1076 (56.7%)

Demographics: 559/1076 (52%) male; median age 52

Exposure history: 30/1076 (2.8%) known exposure within 2 weeks

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated bo VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Marx 2021 (h) (Continued)

Threshold predefined: As for reference sample

Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b] Uninterpretable results: Insufficient saliva 4.6% Indeterminate results: None reported
Comparative	
Notes	Funding: Not stated Publication status: Pre-print (not peer-reviewed) Source: medRxiv Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

Marx 2021 (h) (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (i)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076)
	Recruitment: Unclear
	Prospective or retrospective: Unclear. Probably prospective
	Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%)
	Additional inclusion criteria: None

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (i) (Continued)

Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 610/1076 (56.7%) Demographics: 559/1076 (52%) male; median age 52 Exposure history: 30/1076 (2.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated. CDC Guideline stated VTM. Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic NAT extraction method: Not stated Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity Blinding reported: NS Threshold predefined: Yes Index Sample (A): Saliva swab Sample collection device: Not stated Sample collected by: Supervised patient collection/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated; CDC Guideline stated bo VTM. Timing of sample collection: As for reference sample NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: As for reference sample Threshold predefined: As for reference sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (i) (Continued)

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (i) (Continued)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (j)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (j) (Continued)

Dates: August-November 2020

Symptoms and severity: 610/1076 (56.7%)

Demographics: 559/1076 (52%) male; median age 52

Exposure history: 30/1076 (2.8%) known exposure within 2 weeks

Index tests
Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated bo VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)
Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Marx 2021 (j) (Continued)

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			

Marx 2021 (j) (Continued)

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (k)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 610/1076 (56.7%)

Marx 2021 (k) (Continued)

Demographics: 559/1076 (52%) male; median age 52

Exposure history: 30/1076 (2.8%) known exposure within 2 weeks

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated bo VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

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Marx 2021 (k) (Continued)

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			

Marx 2021 (k) (Continued)

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Marx 2021 (l)

Study characteristics

Patient Sampling Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076)

Recruitment: Unclear

Prospective or retrospective: Unclear. Probably prospective

Sample size (cases): Nasal: 74/932 (8%)
Saliva: 69/864 (8%)

Additional inclusion criteria: None

Patient characteristics and setting Setting: Mixed hospital (A&E and 'other')

Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia)

Country: USA and Georgia

Dates: August-November 2020

Symptoms and severity: 610/1076 (56.7%)

Demographics: 559/1076 (52%) male; median age 52

Exposure history: 30/1076 (2.8%) known exposure within 2 weeks

Index tests **Reference sample:** NP swab

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Marx 2021 (I) (Continued)

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Saliva swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated; CDC Guideline stated bo VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Marx 2021 (I) (Continued)

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			
Are there concerns that the target condition as defined by the reference standard does not match the question?			

Marx 2021 (l) (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Marx 2021 (m)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 610/1076 (56.7%) Demographics: 559/1076 (52%) male; median age 52 Exposure history: 30/1076 (2.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted

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Marx 2021 (m) (Continued)

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

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Marx 2021 (m) (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Oral rinse)			

Marx 2021 (m) (Continued)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Marx 2021 (n)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 610/1076 (56.7%) Demographics: 559/1076 (52%) male; median age 52

Marx 2021 (n) (Continued)

Exposure history: 30/1076 (2.8%) known exposure within 2 weeks

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Marx 2021 (n) (Continued)

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			

Marx 2021 (n) (Continued)

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Marx 2021 (o)

Study characteristics

Patient Sampling

Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076)

Recruitment: Unclear

Prospective or retrospective: Unclear. Probably prospective

Sample size (cases): Nasal: 74/932 (8%)
Saliva: 69/864 (8%)

Additional inclusion criteria: None

Patient characteristics and setting

Setting: Mixed hospital (A&E and 'other')

Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia)

Country: USA and Georgia

Dates: August-November 2020

Symptoms and severity: 610/1076 (56.7%)

Demographics: 559/1076 (52%) male; median age 52

Exposure history: 30/1076 (2.8%) known exposure within 2 weeks

Index tests **Reference sample:** NP swab

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Marx 2021 (o) (Continued)

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Marx 2021 (o) (Continued)

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			
Are there concerns that the target condition as defined by the reference standard does not match the question?			

Marx 2021 (o) (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk

Marx 2021 (p)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 610/1076 (56.7%) Demographics: 559/1076 (52%) male; median age 52 Exposure history: 30/1076 (2.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted

Marx 2021 (p) (Continued)

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

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Marx 2021 (p) (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			
Are there concerns that the target condition as defined by the reference standard does not match the question?			
DOMAIN 4: Flow and timing			
Was there an appropriate interval between index tests?	Yes		

Marx 2021 (p) (Continued)

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk

Marx 2021 (q)

Study characteristics

Patient Sampling	Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076) Recruitment: Unclear Prospective or retrospective: Unclear. Probably prospective Sample size (cases): Nasal: 74/932 (8%) Saliva: 69/864 (8%) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Mixed hospital (A&E and 'other') Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia) Country: USA and Georgia Dates: August-November 2020 Symptoms and severity: 610/1076 (56.7%) Demographics: 559/1076 (52%) male; median age 52 Exposure history: 30/1076 (2.8%) known exposure within 2 weeks
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted Sample collection method: Not stated (specimens were collected according to current CDC guidelines). Sample storage/transport: Not stated. CDC Guideline stated VTM.

Marx 2021 (q) (Continued)

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Marx 2021 (q) *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all pa-	Yes

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Marx 2021 (q) (Continued)

tients receive all index tests (samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)?

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Marx 2021 (r)

Study characteristics

Patient Sampling

Design: Single-group asymptomatic and symptomatic adults enrolled in clinical settings at a large public hospital (n = 1076)

Recruitment: Unclear

Prospective or retrospective: Unclear. Probably prospective

Sample size (cases): Nasal: 74/932 (8%)
Saliva: 69/864 (8%)

Additional inclusion criteria: None

Patient characteristics and setting

Setting: Mixed hospital (A&E and 'other')

Location: Community events (Denver, Colorado), Grady Memorial Hospital (Atlanta, Georgia)

Country: USA and Georgia

Dates: August-November 2020

Symptoms and severity: 610/1076 (56.7%)

Demographics: 559/1076 (52%) male; median age 52

Exposure history: 30/1076 (2.8%) known exposure within 2 weeks

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: 0-7; 8-14 and > 14 days for symptomatic

NAT extraction method: Not stated

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Marx 2021 (r) (Continued)

Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay

Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient collection/HCW-interpreted

Sample collection method: Not stated (specimens were collected according to current CDC guidelines).

Sample storage/transport: Not stated. CDC Guideline stated VTM.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Results for all 3 specimen types available for 1320/1806 (73.1%) participants across Marx [a] and Marx [b]

Uninterpretable results: Insufficient saliva 4.6%

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Pre-print (not peer-reviewed)

Source: medRxiv

Author COI: No COI statement reported

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Marx 2021 (r) (Continued)

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Marx 2021 (r) (Continued)

Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk

Matic 2021

Study characteristics

Patient Sampling	Design: Single group of patients under investigation for COVID-19 from various clinical settings Recruitment: Unclear: 'From March–May 2020, paired saliva and nasopharyngeal swabs were received from patients under investigation for COVID-19 from various clinical settings: inpatients, residents of long-term care (LTC) facilities, healthcare workers, and outpatients.'
Patient characteristics and setting	Setting: Mixed (inpatients, residents of long-term care (LTC) facilities, healthcare workers, and outpatients) Location: Not stated Country: Canada Dates: March to May 2020 Symptoms and severity: 13/74 (17.6%) symptomatic patients requiring admission to a tertiary acute care hospital
Index tests	Reference sample: Nasopharyngeal swab Sample collection device: Not stated Sample collected by: Healthcare worker Sample collection method: swabs were collected using COPAN Flocked Swabs Sample storage/transport: 2 mL of Universal Transport Medium™ (COPAN, Brescia, Italy) or 3 mL of BD™ Universal Viral Transport System (Becton Dickinson, Sparks, MD) Timing of sample collection: Not stated NAT extraction method: MagNA Pure 96 System (Roche Molecular Diagnostics, CA, USA) Assay used: Threshold: LightMix® ModularDx SARS-CoV (COVID19) E-gene assay (TIB Molbiol, Germany) or the cobas® SARS-CoV-2 Test (Roche Molecular Diagnostics, Laval, QC) Index Sample: Saliva spit

Matic 2021 (Continued)

Sample collection device: Sterile screw-top container (Starplex Scientific Inc., Etobicoke, Canada)

Sample collected by: Unsupervised patient

Sample collection method: Patients were asked to provide approximately 1 mL of saliva by pooling saliva in the mouth and spitting into a sterile screw-top container.

Sample storage/transport: Dry/direct sampling. Saliva samples were transported to the laboratory at room temperature without the addition of transport media. In the laboratory, samples were diluted 1:2 with sterile phosphate-buffered saline.

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: 31 samples excluded due to insufficient volume and 1 sample for being a sputum sample

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published paper

Source: European Journal of Clinical Microbiology and Infectious Diseases

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear

Matic 2021 (Continued)

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	No
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	No
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Matic 2021 (Continued)

Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

McCormick-Baw 2020
Study characteristics

Patient Sampling	Two-group study to estimate agreement between NP and saliva samples Design: Total 156 (50) individuals [1] (suspected) cohort tested on the basis of national or institutional guidelines for COVID-19 enriched with cohort, [2] individuals not requiring mechanical ventilation tested whilst an inpatient in a COVID-19 unit (presumed D+). Not able to disaggregate [1] and [2]. Recruitment: [1] "The specimens were collected in the ED, when a patient with suspected COVID-19 was being investigated", [2] "Selected randomly in the hospital COVID unit" Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Hospital inpatient + A&E Location: University of Texas Southwestern Medical Center, Dallas, Texas Country: USA Dates: Not stated Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample:: Nasopharyngeal (NP) Sample collected by: Not stated Sample collection method: "Testing was performed according to the manufacturer's instructions". Sample storage/transport: UTM (5 mL) "Once specimens were collected, they were labelled with a demographic label, double-bagged and submitted to the laboratory through the pneumatic tube system" and were processed 'on demand'. Timing of sample collection: Not stated NAT extraction method: "The liquid, non-viscous components of each specimen were drawn into a disposable pipette (300 uL) issued with the Xpert SARS-CoV-2 cartridges and directly inoculated and run according to the manufacturer's instructions". Assay used: Cepheid Xpert Xpress SARS-CoV-2 PCR test (Sunnyvale, CA)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

McCormick-Baw 2020 (Continued)

Genetic target: E, N2

Threshold: Detection of E and N2, or N2 alone was considered positive.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva

Sample collected by: HCW (nursing staff)

Sample collection method: "Education to the ED nursing staff and the nurses in the COVID-19 unit was disseminated to encourage saliva, not sputum collection". Un-preserved saliva samples (5 mL) were collected in sterile urine cups or sterile 50 mL conical tubes.

Sample storage/transport: "Once specimens were collected, they were labelled with a demographic label, double-bagged and submitted to the laboratory through the pneumatic tube system".

'Saliva samples were held at 2-8 °C for up to 12 hours prior to testing'.

Timing of sample collection: Not stated

NAT extraction method: As for Reference sample

Assay used: As for Reference sample

Genetic target: As for Reference sample

Threshold: As for Reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Paired; no further details provided

All patients received all sampling methods: Not stated

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding received

Publication status: Published paper

Source: Academic journal

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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McCormick-Baw 2020 (Continued)

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Unclear
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

McCormick-Baw 2020 (Continued)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Unclear risk

McCulloch 2020

Study characteristics

Patient Sampling	Two-group study to estimate agreement between NP and nasal mid-turbinate samples for the diagnosis of COVID-19 Design: 158 (18) [1] Symptomatic healthcare workers presenting to drive-through clinics [2] 27 symptomatic outpatients testing SARS-CoV-2 positive presenting for care in primary care or the ED not included in this review Only group 1 was included in the analysis. Recruitment: March 31 to April 13, 2020 Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Community: Drive-through SARS-CoV-2 testing clinics at Harborview Medical Centre Location: University of Washington, Seattle Country: USA Dates: March 31 to April 13 Symptoms and severity: 158 (100%) symptomatic. No further details

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McCulloch 2020 (Continued)

	Demographics: Not stated
	Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: medical assistants and nurses Sample collection method: Swab; no details provided Sample storage/transport: Not stated Timing of sample collection: Median of 2 days between symptom onset and NP swab (range from 1 to 5 days) across groups [1] and [2] NAT extraction method: Roche Magna Pure 96, Viral NA small volume kit Assay used: One step RT-PCR. AgPath-ID system master mix on the real-time ABI 7500 instrument. Developed in-house Genetic target: N1 and N2 Threshold: Amplification of both N-gene targets results in a positive result, amplification of one results in an inconclusive result, and amplification of neither results in a negative result. Blinding reported: Not stated Threshold predefined: Yes Index Sample: Nasal Sample collection device: Flocked mid-nasal swab (Copan FloqSwab 56380CS01, Copan Diagnostics, Murrieta, CA) Sample collected by: Patient was provided with written instructions. Sample collection method: Flocked mid-nasal swab. No further details Sample storage/transport: Universal Transport Media (UTM) (Becton Dickinson, Franklin, NJ) Timing of sample collection: Median of 2 days between symptom onset and NP swab (range from 1 to 5 days) (across groups 1 and 2) NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for reference sample Blinding reported: Not stated Threshold predefined: Yes
Target condition and reference standard(s)	
Flow and timing	Sampling schedule prespecified: Time interval between sampling methods across groups [1] and [2]: Median 0, range -4 to 7 days All patients received all sampling methods: Not stated

McCulloch 2020 (Continued)

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 1 inconclusive NP swab and 6 inconclusive mid-nasal swabs

Comparative

Notes

Funding: None reported

Publication status: Published

Source: Journal of Clinical Virology

Author COI: The authors declared no conflict of interest.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		

McCulloch 2020 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Unclear
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

McLennan 2022

Study characteristics

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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McLennan 2022 (Continued)

Patient Sampling

Design: [1] Single group of NHS Lothian Health Care Workers (HCWs) or their symptomatic household contacts attending the drive-through NHS Lothian COVID-19 testing Centre

[2] Subsample of 19+ and 6- samples from NHS Lothian Health Care Workers (HCWs) or their symptomatic household contacts attending the drive-through NHS Lothian COVID-19 testing Centre (not extracted)

[3] Single group of NHS Lothian Health Care Workers (HCWs) or their symptomatic household contacts attending the drive-through NHS Lothian COVID-19 testing Centre: Random sample of 37+ and 30- samples (not extracted)

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): 109 (11)

Additional inclusion criteria: Children under the age of 5 years were excluded.

Patient characteristics and setting

Setting: COVID-19 testing centre/drive-through

Location: Chalmers Hospital, Edinburgh

Country: UK

Dates: 20-22 May 2020

Symptoms and severity: Not stated

Demographics: Age: Mean (SD): 40.2 (1.2)

Sex: 29/109 (26.6%) male

Exposure history: Not stated

Index tests

Reference sample: Mixed NP/OP

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: Taken before saliva and gargle samples. No further details

Sample storage/transport: Specimens were transported to the lab by cold chain in cool-boxes with ice packs.

Timing of sample collection: NS

NAT extraction method: Omega Biotek MAG-BIND® VIRAL DNA/RNA kit

Assay used: Thermofisher TaqPath CE-IVD kits

Genetic target: N, ORF and S genes

Threshold: NS

Blinding reported: NS

Threshold predefined: Not stated

Index Sample: Saliva spit

Sample collection device: Universal specimen container

McLennan 2022 (Continued)

Sample collected by: Unsupervised patient. A written information leaflet was provided to each eligible attendee and verbal consent for involvement was obtained prior to participation in the study.

Sample collection method: Those who agreed to take part were asked to produce a saliva sample by repeatedly pooling saliva in their mouth and spitting into a universal specimen container.

Sample storage/transport: Dry/direct sampling. Samples treated with proteinase K. Specimens were transported to the lab by cold chain in cool-boxes with ice packs.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: 1 NP/OP and 8 saliva samples had amplification failures.

Indeterminate results: 1 saliva sample inconclusive

Comparative

Notes

Funding: NHS Laboratories Programme COVID-19 innovation saliva testing short-life working group

Publication status: Pre-print

Source: MedRxiv

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		

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McLennan 2022 (Continued)

Was the intention that patients receive all tests at all time points? Yes

Could the selection of patients have introduced bias?

Unclear risk

Are there concerns that the included patients and setting do not match the review question?

Low concern

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? No

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? No

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias?

High risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

McLennan 2022 (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Melo Costa 2021 (a)

Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals admitted to the hospital for SARS-CoV-2 routine diagnosis (group of previously tested not extracted for this review) Recruitment: Consecutive (all individuals on demand of SARS-CoV-2 detection using NPS, accepting in parallel, saliva collection) Prospective or retrospective: Prospective Sample size (cases): MIXED symptomatic and asymptomatic: 273 (46) Asymptomatic: 183 (17) Symptomatic: 90 (29) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Unclear (hospital setting) Location: Institut Hospitalo-Universitaire (IHU) Méditerranée Infection, Marseille Country: France Dates: 6 October 2020 to 16 October 2020 Symptoms and severity: Symptomatic: 90 (33%) Demographics: Symptomatic: Median age 41 (IQR 28.3-50.0) 35 (38.9%) male Asymptomatic: Median age 39 (IQR 28.5-49.5) 98 (50.8%) male Exposure history: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Melo Costa 2021 (a) (Continued)

Index tests

Reference sample: NP swab

Sample collection device: Nasal swabs with viral transport medium (ref. #903,101, Pacific Laboratory Products, Blackburn, Australia)

Sample collected by: Not stated

Sample collection method: Collected with nasal swabs with VTM as following manufacturer's protocol

Sample storage/transport: VTM. Samples were refrigerated on ice at the collection site and stored in these conditions until they arrived in the laboratory. The storing time never exceeded 6 hours.

Timing of sample collection For symptomatic group, median 3 (IQR 1-5) days pso

NAT extraction method: NucleoMag® Pathogen Isolation kit (MACHEREY NAGEL GmbH & Co, Düren, Germany) using the KingFisher™ Flex system (ThermoFisher Scientific, Villebon Courtaboeuf, France)

Assay used: Protocol not stated, performed in a LightCycler 480II instrument (Roche Diagnostics®, Mannheim, Germany)

Genetic target: E gene

Threshold: Ct value < 35 as positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Cotton roll (Neutral Salivettes®, SARSTEDT, Numbrecht, Germany)

Sample collected by: Patient supervised by laboratory technician

Sample collection method: Each participant should not have eaten or drunk anything in the 30 minutes prior to saliva collection.

Collected with a cotton roll (Neutral Salivettes®, SARSTEDT, Numbrecht, Germany) directly introduced into the mouth without handling and then kept for 2 min in the participant's mouth who soaked the cotton by doing circular movements, prior to replacing it into the stopper part of the Salivette® tube

Sample storage/transport: Dry sampling.
Ultra-pure water was used if necessary to increase the volume of the sample.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Melo Costa 2021 (a) (Continued)

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the French Defence Innovation Agency - Agence de l'innovation de défense (AID, CoviDiagMS Project) and the French General Armament Directorate - Direction Générale de l'Armement (DGA, MoSIS)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		

Melo Costa 2021 (a) *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Melo Costa 2021 (b)

Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals admitted to the hospital for SARS-CoV-2 routine diagnosis (group of previously tested not extracted for this review) Recruitment: Consecutive (all individuals in demand of SARS-CoV-2 detection using NPS, accepting in parallel, saliva collection) Prospective or retrospective: Prospective Sample size (cases): MIXED symptomatic and asymptomatic: 273 (46) Asymptomatic: 183 (17) Symptomatic: 90 (29) Additional inclusion criteria: None

Patient characteristics and setting	Setting: Unclear (hospital setting) Location: Institut Hospitalo-Universitaire (IHU) Méditerranée Infection, Marseille Country: France Dates: 6 October 2020 to 16 October 2020 Symptoms and severity: Symptomatic: 90 (33%) Demographics: Symptomatic: Median age 41 (IQR 28.3-50.0) 35 (38.9%) male Asymptomatic: Median age 39 (IQR 28.5-49.5) 98 (50.8%) male Exposure history: Not stated

Index tests	Reference sample: NP swab Sample collection device: Nasal swabs with viral transport medium (ref. #903,101, Pacific Laboratory Products, Blackburn, Australia) Sample collected by: Not stated Sample collection method: Collected with nasal swabs with VTM as following manufacturer's protocol Sample storage/transport: VTM. Samples were refrigerated on ice at the collection site and stored in these conditions until they arrived in the laboratory. The storing time never exceeded 6 hours. Timing of sample collection: For symptomatic group, median 3 (IQR 1-5) days pso NAT extraction method: NucleoMag® Pathogen Isolation kit (MACHEREY NAGEL GmbH & Co, Düren, Germany) using the KingFisher™ Flex system (ThermoFisher Scientific, Villebon Courtaboeuf, France) Assay used: Protocol not stated, performed in a LightCycler 480II instrument (Roche Diagnostics®, Mannheim, Germany) Genetic target: E gene Threshold: Ct value < 35 as positivity

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Melo Costa 2021 (b) (Continued)

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Cotton roll (Neutral Salivettes®, SARSTEDT, Numbrecht, Germany)

Sample collected by: Patient supervised by laboratory technician

Sample collection method: Each participant should not have eaten or drunk anything in the 30 minutes prior to saliva collection

Collected with a cotton roll (Neutral Salivettes®, SARSTEDT, Numbrecht, Germany) directly introduced into the mouth without handling and then kept for 2 min in the participant's mouth, who soaked the cotton by doing circular movements, prior to replacing it into the stopper part of the Salivette® tube

Sample storage/transport: Dry sampling.

Ultra-pure water was used if necessary to increase the volume of the sample.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the French Defence Innovation Agency - Agence de l'innovation de défense (AID, CoviDiagMS Project) and the French General Armament Directorate - Direction Générale de l'Armement (DGA, MoSIS project)

Publication status: Published paper

Source: Journal of Oral Microbiology

Author COI: Authors declared no COI present.

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Melo Costa 2021 (b) *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Low risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	

Melo Costa 2021 (b) *(Continued)*

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Melo Costa 2021 (c)
Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals admitted to the hospital for SARS-CoV-2 routine diagnosis (group of previously tested not extracted for this review) Recruitment: Consecutive (all individuals in demand of SARS-CoV-2 detection using NPS, accepting in parallel, saliva collection) Prospective or retrospective: Prospective Sample size (cases): MIXED symptomatic and asymptomatic: 273 (46) Asymptomatic: 183 (17) Symptomatic: 90 (29)
Patient characteristics and setting	Setting: Unclear (hospital setting) Location: Institut Hospitalo-Universitaire (IHU) Méditerranée Infection, Marseille Country: France Dates: 6 October 2020 to 16 October 2020 Symptoms and severity: Symptomatic: 90 (33%) Demographics: Symptomatic: Median age 41 (IQR 28.3-50.0) 35 (38.9%) male Asymptomatic:

Melo Costa 2021 (c) (Continued)

Median age 39 (IQR 28.5-49.5)

98 (50.8%) male

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Nasal swabs with viral transport medium (ref. #903,101, Pacific Laboratory Products, Blackburn, Australia)

Sample collected by: Not stated

Sample collection method: Collected with nasal swabs with VTM as following manufacturer's protocol

Sample storage/transport: VTM. Samples were refrigerated on ice at the collection site and stored in these conditions until they arrived in the laboratory. The storing time never exceeded 6 hours.

Timing of sample collection: For symptomatic group, median 3 (IQR 1-5) days pso

NAT extraction method: NucleoMag® Pathogen Isolation kit (MACHEREY NAGEL GmbH & Co, Düren, Germany) using the KingFisher™ Flex system (ThermoFisher Scientific, Villebon Courtaboeuf, France)

Assay used: Protocol not stated, performed in a LightCycler 480II instrument (Roche Diagnostics®, Mannheim, Germany)

Genetic target: E gene

Threshold: Ct value < 35 as positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Cotton roll (Neutral Salivettes®, SARSTEDT, Numbrecht, Germany)

Sample collected by: Patient supervised by laboratory technician

Sample collection method: Each participant should not have eaten or drunk anything in the 30 minutes prior to saliva collection

Collected with a cotton roll (Neutral Salivettes®, SARSTEDT, Numbrecht, Germany) directly introduced into the mouth without handling and then kept for 2 min in the participant's mouth, who soaked the cotton by doing circular movements, prior to replacing it into the stopper part of the Salivette® tube

Sample storage/transport: Dry sampling.

Ultra-pure water was used if necessary to increase the volume of the sample.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Melo Costa 2021 (c) (Continued)

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the French Defence Innovation Agency - Agence de l'innovation de défense (AID, CoviDiagMS Project) and the French General Armament Directorate - Direction Générale de l'Armement (DGA, MoSIS project)

Publication status: Published paper

Source: Journal of Oral Microbiology

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			

Melo Costa 2021 (c) *(Continued)*
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Mestdagh 2021 (a)[A]
Study characteristics
The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Mestdagh 2021 (a)[A] (Continued)

Patient Sampling	Design: Single group Asymptomatic and symptomatic adults (> 18) suggestive of COVID-19 presenting to test triage centres Laboratory (n = 2850) (note: 104 participants tested not included as NP samples missing) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2469 (118) Additional inclusion criteria: 2954 individuals recruited and 2850 finally included. Missing NP results in 104/2850 of the participants (3.6%)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020 Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status of which 1376/2071 (66%) symptomatic. Demographics: Age: median age group: 31-40 years old Sex: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China). Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions. Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA) Timing of sample collection: Not stated NAT extraction method: Total RNA Purification Kit (Norgen Biotek #24300) according to the manufacturer's instructions Assay used: Taq one-step RT-qPCR mastermix (Bio-Rad, Temse, Belgium) Genetic target: E, ORF1ab, N, S Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (https://www.fda.gov/media/136112/download) Blinding reported: Threshold predefined: Yes Index Sample (A): Saliva spit Sample collection device: 'Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Mestdagh 2021 (a)[A] (Continued)

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: Missing NP swab results from 104/2850 (3.6%) participants tested

Saliva swab samples 'not available': 201/2850 (7%). Saliva spit samples 'not available': 381/2850 (13%)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		

Mestdagh 2021 (a)[A] *(Continued)*

Was the intention that patients receive all tests at all time points? Yes

Could the selection of patients have introduced bias? Unclear risk

Are there concerns that the included patients and setting do not match the review question? Low concern

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Mestdagh 2021 (a)[A] *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? High risk

Mestdagh 2021 (a)[B]
Study characteristics

Patient Sampling	Design: Single group Asymptomatic and symptomatic adults (> 18) suggestive of COVID-19 presenting to test triage centres Laboratory (n = 2850) (note 104 participants tested not included as NP samples missing) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2469 (118) Additional inclusion criteria: 2954 individuals recruited and 2850 finally included. Missing NP results in 104/2850 of the participants (3.6%)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020 Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status of which 1376/2071 (66%) symptomatic. Demographics: Age: median age group: 31-40 years old

Mestdagh 2021 (a)[B] (Continued)

Sex: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China).
Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Total RNA Purification Kit (Norgen Biotek #24300) according to the manufacturer's instructions

Assay used: Taq one-step RT-qPCR mastermix (Bio-Rad, Temse, Belgium)

Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

Blinding reported:

Threshold predefined: Yes

Index Sample (B): Saliva swab/salivate

Sample collection device: Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: Missing NP swab results from 104/2850 (3.6%) participants tested

Mestdagh 2021 (a)[B] (Continued)

Saliva swab samples 'not available': 201/2850 (7%). Saliva spit samples 'not available': 381/2850 (13%)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative
Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

Mestdagh 2021 (a)[B] *(Continued)*

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Unclear
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes

Mestdagh 2021 (a)[B] *(Continued)*

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias?

High risk

Mestdagh 2021 (b)[A]
Study characteristics

Patient Sampling

Design: Single group
Asymptomatic and symptomatic adults (> 18) suggestive of COVID-19 presenting to test triage centres
Laboratory (n = 2850) (note 104 participants tested not included as NP samples missing)

Recruitment: Between June 2020 and July 2020

Prospective or retrospective: Prospective

Sample size (cases): 2469 (118)

Additional inclusion criteria: 2954 individuals recruited and 2850 finally included. Missing NP results in 104/2850 of the participants (3.6%)

Patient characteristics and setting

Setting: COVID-19 testing centre

Location: Triage centres from the Belgian national testing platform

Country: Belgium

Dates: Between June 2020 and July 2020

Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071)
Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic.

Demographics: Age: median age group: 31-40 years old
Sex: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China).
Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Total RNA Purification Kit (Norgen Biotek #24300) according to the manufacturer's instructions
Assay used: Taq one-step RT-qPCR mastermix (Bio-Rad, Temse, Belgium)
Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Mestdagh 2021 (b)[A] (Continued)

Blinding reported:

Threshold predefined: Yes

Index Sample (A): Saliva spit

Sample collection device: 'Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: Missing NP swab results from 104/2850 (3.6%) participants tested

Saliva swab samples 'not available': 201/2850 (7%). Saliva spit samples 'not available': 381/2850 (13%)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Mestdagh 2021 (b)[A] *(Continued)*

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples,	Unclear

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Mestdagh 2021 (b)[A] (Continued)

different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	High risk

Mestdagh 2021 (b)[B]

Study characteristics

Patient Sampling	Design: Single group Asymptomatic and symptomatic adults (> 18) suggestive of COVID-19 presenting to test triage centres Laboratory (n = 2850) (note 104 participants tested not included as NP samples missing) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2469 (118) Additional inclusion criteria: 2954 individuals recruited and 2850 finally included. Missing NP results in 104/2850 of the participants (3.6%)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020 Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic. Demographics: Age: median age group: 31-40 years old Sex: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China). Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Mestdagh 2021 (b)[B] (Continued)

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Total RNA Purification Kit (Norgen Biotek #24300) according to the manufacturer's instructions

Assay used: Taq one-step RT-qPCR mastermix (Bio-Rad, Temse, Belgium)

Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

Blinding reported:

Threshold predefined: Yes

Index Sample (B): Saliva swab/salivate

Sample collection device: Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: Missing NP swab results from 104/2850 (3.6%) participants tested

Saliva swab samples 'not available': 201/2850 (7%). Saliva spit samples 'not available': 381/2850 (13%)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Mestdagh 2021 (b)[B] (Continued)

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			
DOMAIN 3: Reference standard			
Could the reference standard, its conduct, or its interpretation have introduced bias?			

Mestdagh 2021 (b)[B] (Continued)

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? High risk

Mestdagh 2021 (c)[A]

Study characteristics

Patient Sampling	Design: Single group Asymptomatic and symptomatic adults (> 18) suggestive of COVID-19 presenting to test triage centres Laboratory (n = 2850) (note 104 participants tested not included as NP samples missing) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2469 (118) Additional inclusion criteria: 2954 individuals recruited and 2850 finally included. Missing NP results in 104/2850 of the participants (3.6%)
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Mestdagh 2021 (c)[A] (Continued)

Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071)
Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic.

Demographics: Age: median age group: 31-40 years old

Sex: Not stated

Exposure history: Not stated

Index tests
Reference sample: NP swab

Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China).

Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Total RNA Purification Kit (Norgen Biotek #24300) according to the manufacturer's instructions

Assay used: Taq one-step RT-qPCR mastermix (Bio-Rad, Temse, Belgium)

Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

Blinding reported:

Threshold predefined: Yes

Index Sample (A): Saliva spit

Sample collection device: Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)
Flow and timing

Simultaneous sample collection: Unclear

Missing data: Missing NP swab results from 104/2850 (3.6%) participants tested

Mestdagh 2021 (c)[A] (Continued)

Saliva swab samples 'not available': 201/2850 (7%). Saliva spit samples 'not available': 381/2850 (13%)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Mestdagh 2021 (c)[A] (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? High risk

Mestdagh 2021 (c)[B]

Study characteristics

Patient Sampling	Design: Single group Asymptomatic and symptomatic adults (> 18) suggestive of COVID-19 presenting to test triage centres Laboratory (n = 2850) (note 104 participants tested not included as NP samples missing) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2469 (118)

Mestdagh 2021 (c)[B] (Continued)

Additional inclusion criteria: 2954 individuals recruited and 2850 finally included. Missing NP results in 104/2850 of the participants (3.6%)

Patient characteristics and setting

Setting: COVID-19 testing centre

Location: Triage centres from the Belgian national testing platform

Country: Belgium

Dates: Between June 2020 and July 2020

Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071)

Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic.

Demographics: Age: median age group: 31-40 years old

Sex: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China)

Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Total RNA Purification Kit (Norgen Biotek #24300) according to the manufacturer's instructions

Assay used: Taq one-step RT-qPCR mastermix (Bio-Rad, Temse, Belgium)

Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

Blinding reported:

Threshold predefined: Yes

Index Sample (B): Saliva swab/salivate

Sample collection device: Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Mestdagh 2021 (c)[B] (Continued)

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: Missing NP swab results from 104/2850 (3.6%) participants tested. Saliva swab samples 'not available': 201/2850 (7%). Saliva spit samples 'not available': 381/2850 (13%)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?			
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Mestdagh 2021 (c)[B] *(Continued)*
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Unclear

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? High risk

Mestdagh 2021 (d)[A]
Study characteristics

Patient Sampling	Design: Single group
	Laboratory (n = 2526)
	Recruitment: Between June 2020 and July 2020
	Prospective or retrospective: Prospective

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Mestdagh 2021 (d)[A] (Continued)

	Sample size (cases): 2491 (72) Additional inclusion criteria: Lab results provided in suppl. table. The largest sample size reported (above) was for NPS versus saliva swab.
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020 Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic. Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China). Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions. Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA) Timing of sample collection: Not stated NAT extraction method: Magnetic bead-based RNA extraction method developed by University of Liège (CoRNA kit) according to the recommended protocol Assay used: TaqPath COVID-19 Combo Kit (Applied Biosystems) Genetic target: E, ORF1ab, N, S Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (https://www.fda.gov/media/136112/download) Blinding reported: NS Threshold predefined: Yes Index Sample (A): Saliva spit Sample collection device: Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada Sample collected by: Supervised patient-collected/laboratory staff-interpreted Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions. Sample storage/transport: As for reference sample

Mestdagh 2021 (d)[A] (Continued)

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Mestdagh 2021 (d)[A] *(Continued)*

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes

Mestdagh 2021 (d)[A] *(Continued)*

Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Mestdagh 2021 (d)[B]
Study characteristics

Patient Sampling	Design: Single group Laboratory (n = 2526) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2491 (72) Additional inclusion criteria: Lab: Results provided in suppl. table. The largest sample size reported (above) was for NPS versus saliva swab.
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020 Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic. Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China). Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions. Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA) Timing of sample collection: Not stated

Mestdagh 2021 (d)[B] (Continued)

NAT extraction method: Magnetic bead-based RNA extraction method developed by University of Liège (CoRNA kit) according to the recommended protocol

Assay used: TaqPath COVID-19 Combo Kit (Applied Biosystems)

Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Saliva swab/salivate

Sample collection device: Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Mestdagh 2021 (d)[B] (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Mestdagh 2021 (d)[B] (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Mestdagh 2021 (e)[A]

Study characteristics

Patient Sampling	Design: Single group Laboratory (n = 2526) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2491 (72) Additional inclusion criteria: Lab results provided in suppl. table. The largest sample size reported (above) was for NPS versus saliva swab.
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020

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Mestdagh 2021 (e)[A] *(Continued)*

Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071)
Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic.

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China)

Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Magnetic bead-based RNA extraction method developed by University of Liège (CoRNA kit) according to the recommended protocol

Assay used: TaqPath COVID-19 Combo Kit (Applied Biosystems)

Genetic target: E, ORF1ab, N, S

Index Sample (A): Saliva spit

Sample collection device: 'Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Mestdagh 2021 (e)[A] (Continued)

Flow and timing

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			

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Mestdagh 2021 (e)[A] *(Continued)*
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Mestdagh 2021 (e)[B]
Study characteristics

Patient Sampling	Design: Single group
	Laboratory (n = 2526)
	Recruitment: Between June 2020 and July 2020
	Prospective or retrospective: Prospective
	Sample size (cases): 2491 (72)
	Additional inclusion criteria: Lab results provided in suppl. table. The largest sample size reported (above) was for NPS versus saliva swab.
Patient characteristics and setting	Setting: COVID-19 testing centre
	Location: Triage centres from the Belgian national testing platform
	Country: Belgium

Mestdagh 2021 (e)[B] (Continued)

Dates: Between June 2020 and July 2020

Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071)

Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic.

Demographics: Not stated

Exposure history: Not stated

Index tests
Reference sample: NP swab

Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China).

Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Magnetic bead-based RNA extraction method developed by University of Liège (CoRNA kit) according to the recommended protocol

Assay used: TaqPath COVID-19 Combo Kit (Applied Biosystems)

Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Saliva swab/salivate

Sample collection device: Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Mestdagh 2021 (e)[B] (Continued)

Target condition and reference
standard(s)

Flow and timing	Simultaneous sample collection: Unclear
	Missing data: None reported
	Uninterpretable results: None reported
	Indeterminate results: None reported

Comparative

Notes	Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Scien- sano, Brussels, Belgium
	Publication status: Published paper
	Source: Journal of Molecular Diagnostics
	Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?	Unclear

Was a case-control design avoid- ed?	Yes

Did the study avoid inappropriate exclusions?	Unclear

Did the study avoid inappropriate inclusions?	Unclear

Was the intention that patients receive all tests at all time points?	Yes

Could the selection of patients have introduced bias?	Unclear risk

Are there concerns that the in- cluded patients and setting do not match the review question?	Low concern

DOMAIN 2: Index test (Saliva)
DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
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Mestdagh 2021 (e)[B] *(Continued)*
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Mestdagh 2021 (f)[A]
Study characteristics

Patient Sampling Design: Single group
Laboratory (n = 2526)
Recruitment: Between June 2020 and July 2020
Prospective or retrospective: Prospective

Mestdagh 2021 (f)[A] (Continued)

	Sample size (cases): 2491 (72) Additional inclusion criteria: Lab results provided in suppl. table. The largest sample size reported (above) was for NPS versus saliva swab.
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020 Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic. Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China) Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions. Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA) Timing of sample collection: Not stated NAT extraction method: Magnetic bead-based RNA extraction method developed by University of Liège (CoRNA kit) according to the recommended protocol Assay used: TaqPath COVID-19 Combo Kit (Applied Biosystems) Genetic target: E, ORF1ab, N, S Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (https://www.fda.gov/media/136112/download) Blinding reported: NS Threshold predefined: Yes Index Sample (A): Saliva spit Sample collection device: 'Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada Sample collected by: Supervised patient-collected/laboratory staff-interpreted Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions. Sample storage/transport: As for reference sample Timing of sample collection: Not stated NAT extraction method: As for reference sample Assay used: As for reference sample

Mestdagh 2021 (f)[A] (Continued)

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Index Sample (B): Saliva swab/salivate

Sample collection device: Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Sciensano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality
Item
Authors' judgement
Risk of bias
Applicability concerns
DOMAIN 1: Patient selection

Mestdagh 2021 (f)[A] *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	

Mestdagh 2021 (f)[A] *(Continued)*

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Mestdagh 2021 (f)[B]
Study characteristics

Patient Sampling	Design: Single group Laboratory (n = 2526) Recruitment: Between June 2020 and July 2020 Prospective or retrospective: Prospective Sample size (cases): 2491 (72) Additional inclusion criteria: Lab results provided in suppl. table. The largest sample size reported (above) was for NPS versus saliva swab.
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Triage centres from the Belgian national testing platform Country: Belgium Dates: Between June 2020 and July 2020 Symptoms and severity: 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic. Demographics: Not stated Exposure history: Not stated

Mestdagh 2021 (f)[B] (Continued)

Index tests

Reference sample: NP swab

Sample collection device: iClean NP swabs (Chenyang Global, Shenzhen, China)

Sample collected by: HCW or trained non-HCW-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Collection was made according to the manufacturer's instructions.

Sample storage/transport: Samples were collected in a transport buffer that inactivated the virus and stabilised the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)

Timing of sample collection: Not stated

NAT extraction method: Magnetic bead-based RNA extraction method developed by University of Liège (CoRNA kit) according to the recommended protocol

Assay used: TaqPath COVID-19 Combo Kit (Applied Biosystems)

Genetic target: E, ORF1ab, N, S

Threshold: 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (<https://www.fda.gov/media/136112/download>)

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Saliva swab/salivate

Sample collection device: Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada

Sample collected by: Supervised patient-collected/laboratory staff-interpreted

Sample collection method: Patients were asked not to eat, drink, smoke or use chewing gum in the previous 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to the manufacturer's instructions.

Sample storage/transport: As for reference sample

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference
standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Mestdagh 2021 (f)[B] (Continued)

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by the VALCOR (Validation of SARS-CoV-2 Assays) project, funded by Scien-sano, Brussels, Belgium

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sam-ple of patients enrolled?	Unclear		
Was a case-control design avoid-ed?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients re-ceive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the in-cluded patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			
DOMAIN 2: Index test (Operator)			

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Mestdagh 2021 (f)[B] (Continued)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Miguères 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and saliva samples for the diagnosis of COVID-19 Design: 114 ambulatory and 9 hospitalised symptomatic and asymptomatic patients: 123 (44) Recruitment: Not stated Prospective or retrospective: Not stated
Patient characteristics and setting	Setting: Mixed in and outpatient Location: CHU, Purpan, Toulouse Country: France Dates: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Migueres 2020 (Continued)

Symptoms and Severity: Not stated for whole sample. Of 44 with ≥ 1 +ve sample: 17 (39%) asymptomatic, 27 (61%) symptomatic (9/27 hospitalised). Of symptomatic, 19 were ≤ 1 week post-onset, and 8 > 1 week.

Demographics:

Median age: 43 y

Sex: 49 (40% male)

Index tests
Reference Sample: Nasopharyngeal (NP)

Sample collected by: Not stated

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: For symptomatic, 19/27 with ≥ 1 +ve result were within 1 week of symptom onset.

NAT extraction method: Not stated

Assay used: RT-PCR (Hologic, Panther Fusion)

Genetic target: SARS-CoV-2 RNA dependent polymerase gene (IP2, IP4, Institut Pasteur, Paris, France).

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Presume yes (commercial kit used)

Index Sample: Saliva

Sample collection device: Not stated

Sample collected by: Self-collected

Sample collection method: Patients asked to salivate, swirl the saliva around their mouth for at least 30 s and then spit into a sterile container.

Sample storage/transport: Not stated

Timing of sample collection: For symptomatic, 19/27 with ≥ 1 +ve result were within 1 week of symptom onset.

NAT extraction method: As for reference sample

Genetic target: As for reference sample

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Presume yes (commercial kit used)

Target condition and reference standard(s)
Flow and timing

Sampling schedule prespecified: Unclear

Time interval between sampling methods: same day

All patients received all sampling methods: Yes

Missing data: None reported

Miguères 2020 (Continued)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Gates Venture

Publication status: Published Paper

Source: JAMA Network Open

Author COI: Authors received research funding from several pharmaceutical companies; not related with the study objective

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Migueres 2020 (Continued)

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Migueres 2021 (a)
Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre
	Recruitment: Unclear (27 to 29 October 2020)
	Prospective or retrospective: Prospective

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Migueres 2021 (a) (Continued)

	Sample size (cases): 301 (55) Additional inclusion criteria: 2/303 samples were noted as indeterminate results. It is unclear whether these were from symptomatic or asymptomatic individuals. Excluded from analysis
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Toulouse University Hospital, Toulouse Country: France Dates: 27 to 29 October 2020 Symptoms and severity: 160/303 (52.8%) mildly symptomatic Demographics: Age: Mean 33 (range 3-77 yrs) Sex: 144/303 (47.5%) male (across Migueres 2021 (a) and Migueres 2021 (b)) Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Flocked swab (Virus sampling kit, Yocon, Beijing, China) Sample collected by: Healthcare worker (HCW) Sample collection method: NPs were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM) Sample storage/transport: Viral Transport Medium (VTM). All samples were tested in the clinical laboratory within 24 hours after collection. Timing of sample collection: Not stated NAT extraction method: Aptima lysis tube Assay used: Laboratory-developed test (LDT) based on real-time RT-PCR on a Panther Fusion module (Hologic, San Diego, California) Genetic target: ORF1ab gene RdRp gene Threshold: Ct > 35 for positivity Blinding reported: NS Threshold predefined: Yes Index Sample: Saliva spit Sample collection device: Not stated Sample collected by: Supervised patient/supervised parent Sample collection method: Saliva (1 mL) was collected after the subjects had swilled their saliva around their mouths for at least 30 seconds and then spitting into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM). Sample storage/transport: Minimum Essential Media (MEM) Timing of sample collection: Not stated NAT extraction method: As for reference sample

Migueres 2021 (a) (Continued)

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 2/303 (0.6%) saliva samples provided an indeterminate result.

Comparative

Notes

Funding: Hologic provided the molecular reagents for SARS-CoV-2 detection.

Publication status: Published paper

Source: Diagnostic Microbiology and Infectious Diseases

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Migueres 2021 (a) *(Continued)*

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No

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Migueres 2021 (a) *(Continued)*

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Migueres 2021 (b)

Study characteristics	
Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre Recruitment: Unclear (27 to 29 October 2020) Prospective or retrospective: Prospective Sample size (cases): 301(56) Additional inclusion criteria: 2/303 samples were noted as indeterminate results. It is unclear whether these were from symptomatic or asymptomatic individuals. Excluded from analysis
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Toulouse University Hospital, Toulouse Country: France Dates: 27 to 29 October 2020 Symptoms and severity: 160/303 (52.8%) mildly symptomatic Demographics: Age: Mean 33 (range 3-77 yrs) Sex: 144/303 (47.5%) male (across Migueres 2021 (a) and Migueres 2021 (b)) Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Flocked swab (Virus sampling kit, Yocon, Beijing, China) Sample collected by: Healthcare worker (HCW) Sample collection method: NPs were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM) Sample storage/transport: Viral Transport Medium (VTM). All samples were tested in the clinical laboratory within 24 hours after collection. Timing of sample collection: Not stated NAT extraction method: Aptima lysis tube Assay used: Laboratory-developed test (LDT) based on real-time RT-PCR on a Panther Fusion module (Hologic, San Diego, California) Genetic target: ORF1ab gene RdRp gene Threshold: Ct > 35 for positivity

Migueres 2021 (b) (Continued)

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Not stated

Sample collected by: Supervised patient/supervised parent

Sample collection method: Saliva (1 mL) was collected after the subjects had swilled their saliva around their mouths for at least 30 seconds and then spitting into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM)

Sample storage/transport: Minimum Essential Media (MEM)

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 2/303 (0.6%) saliva samples provided an indeterminate result.

Comparative

Notes

Funding: Hologic provided the molecular reagents for SARS-CoV-2 detection.

Publication status: Published paper

Source: Diagnostic Microbiology and Infectious Diseases

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		

Migueres 2021 (b) *(Continued)*

Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes

Migueres 2021 (b) (Continued)

Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Migueres 2021 (c)

Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre Recruitment: Unclear (27 to 29 October 2020) Prospective or retrospective: Prospective Sample size (cases): 301(56) Additional inclusion criteria: 2/303 samples were noted as indeterminate results. It is unclear whether these were from symptomatic or asymptomatic individuals. Excluded from analysis
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Toulouse University Hospital, Toulouse Country: France Dates: 27 to 29 October 2020 Symptoms and severity: 160/303 (52.8%) mildly symptomatic Demographics: Age: Mean 33 (range 3-77 yrs) Sex: 144/303 (47.5%) male (across Migueres 2021 (a) and Migueres 2021 (b)) Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Flocked swab (Virus sampling kit, Yocon, Beijing, China) Sample collected by: Healthcare worker (HCW) Sample collection method: NPs were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM) Sample storage/transport: Viral Transport Medium (VTM). All samples were tested in the clinical laboratory within 24 hours after collection. Timing of sample collection: Not stated NAT extraction method: Aptima lysis tube

Migueres 2021 (c) (Continued)

Assay used: Laboratory-developed test (LDT) based on real-time RT-PCR on a Panther Fusion module (Hologic, San Diego, California)

Genetic target: ORF1ab gene RdRp gene

Threshold: Ct > 35 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Not stated

Sample collected by: Supervised patient/supervised parent

Sample collection method: Saliva (1mL) was collected after the subjects had swilled their saliva around their mouths for at least 30 seconds and then spitting into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM).

Sample storage/transport: Minimum Essential Media (MEM)

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 2/303 (0.6%) saliva samples provided an indeterminate result.

Comparative

Notes

Funding: Hologic provided the molecular reagents for SARS-CoV-2 detection.

Publication status: Published paper

Source: Diagnostic Microbiology and Infectious Diseases

Author COI: Authors declared no COI present.

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Migueres 2021 (c) *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on	Yes

Migueres 2021 (c) *(Continued)*

day 1 and day 2 after symptoms on-set), did all patients receive all index tests (samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Migueres 2021 (d)
Study characteristics

Patient Sampling

Design: Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre

Recruitment: Unclear (27 to 29 October 2020)

Prospective or retrospective: Prospective

Sample size (cases): 301 (56)

Additional inclusion criteria: 2/303 samples were noted as indeterminate results. It is unclear whether these were from symptomatic or asymptomatic individuals. Excluded from analysis

Patient characteristics and setting

Setting: COVID-19 testing centre/drive-through

Location: Toulouse University Hospital, Toulouse

Country: France

Dates: 27 to 29 October 2020

Symptoms and severity: 160/303 (52.8%) mildly symptomatic

Demographics: Age: Mean 33 (range 3-77 yrs)

Sex: 144/303 (47.5%) male (across [Migueres 2021 \(a\)](#) and [Migueres 2021 \(b\)](#))

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Flocked swab (Virus sampling kit, Yocon, Beijing, China)

Sample collected by: Healthcare worker (HCW)

Sample collection method: NPs were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM)

Migueres 2021 (d) (Continued)

Sample storage/transport: Viral Transport Medium (VTM). All samples were tested in the clinical laboratory within 24 hours after collection.

Timing of sample collection: Not stated

NAT extraction method: Aptima lysis tube

Assay used: Laboratory-developed test (LDT) based on real-time RT-PCR on a Panther Fusion module (Hologic, San Diego, California)

Genetic target: ORF1ab gene RdRp gene

Threshold: Ct > 35 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Not stated

Sample collected by: Supervised patient/supervised parent

Sample collection method: Saliva (1 mL) was collected after the subjects had swilled their saliva around their mouths for at least 30 seconds and then spitting into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM).

Sample storage/transport: Minimum Essential Media (MEM)

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 2/303 (0.6%) saliva samples provided an indeterminate result.

Comparative

Notes

Funding: Hologic provided the molecular reagents for SARS-CoV-2 detection.

Publication status: Published paper

Source: Diagnostic Microbiology and Infectious Diseases

Author COI: Authors declared no COI present.

Migueres 2021 (d) (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			

Migueres 2021 (d) (Continued)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Migueres 2021 (e)

Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre Recruitment: Unclear (27 to 29 October 2020) Prospective or retrospective: Prospective Sample size (cases): 301 (55) Additional inclusion criteria: 2/303 samples were noted as indeterminate results. It is unclear whether these were from symptomatic or asymptomatic individuals. Excluded from analysis
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Toulouse University Hospital, Toulouse Country: France

Migueres 2021 (e) *(Continued)*

Dates: 27 to 29 October 2020

Symptoms and severity: 160/303 (52.8%) mildly symptomatic

Demographics: Age: Mean 33 (range 3-77 yrs)

Sex: 144/303 (47.5%) male (across [Migueres 2021 \(a\)](#) and [Migueres 2021 \(b\)](#))

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Flocked swab (Virus sampling kit, Yocon, Beijing, China)

Sample collected by: Healthcare worker (HCW)

Sample collection method: NPs were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM)

Sample storage/transport: Viral Transport Medium (VTM). All samples were tested in the clinical laboratory within 24 hours after collection.

Timing of sample collection: Not stated

NAT extraction method: Aptima lysis tube

Assay used: Aptima SARS-CoV-2 transcription-mediated amplification assay (TMA) (Hologic, San Diego, California)

Genetic target: ORF1ab gene, RdRp gene

Threshold: Ct > 35 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Not stated

Sample collected by: Supervised patient/supervised parent

Sample collection method: Saliva (1 mL) was collected after the subjects had swilled their saliva around their mouths for at least 30 seconds and then spitting into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM).

Sample storage/transport: Minimum Essential Media (MEM)

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Migueres 2021 (e) *(Continued)*

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 2/303 (0.6%) saliva samples provided an indeterminate result.

Comparative

Notes

Funding: Hologic provided the molecular reagents for SARS-CoV-2 detection.

Publication status: Published paper

Source: Diagnostic Microbiology and Infectious Diseases

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
DOMAIN 2: Index test (Oral rinse)			

Migueres 2021 (e) (Continued)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias?

Migueres 2021 (f)

Study characteristics

Patient Sampling	Design: Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre Recruitment: Unclear (27 to 29 October 2020) Prospective or retrospective: Prospective Sample size (cases): 301 (55) Additional inclusion criteria: 2/303 samples were noted as indeterminate results. It is unclear whether these were from symptomatic or asymptomatic individuals. Excluded from analysis
Patient characteristics and setting	Setting: COVID-19 testing centre/drive-through Location: Toulouse University Hospital, Toulouse

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Migueres 2021 (f) (Continued)

Country: France

Dates: 27 to 29 October 2020

Symptoms and severity: 160/303 (52.8%) mildly symptomatic

Demographics: Age: Mean 33 (range 3-77 yrs)

Sex: 144/303 (47.5%) male (across [Migueres 2021 \(a\)](#) and [Migueres 2021 \(b\)](#))

Exposure history: Not stated

Index tests

Reference sample: NP swab

Sample collection device: Flocked swab (Virus sampling kit, Yocon, Beijing, China)

Sample collected by: Healthcare worker (HCW)

Sample collection method: NPs were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM).

Sample storage/transport: Viral Transport Medium (VTM). All samples were tested in the clinical laboratory within 24 hours after collection.

Timing of sample collection: Not stated

NAT extraction method: Aptima lysis tube

Assay used: Aptima SARS-CoV-2 transcription-mediated amplification assay (TMA) (Hologic, San Diego, California)

Genetic target: ORF1ab gene, RdRp gene

Threshold: Ct > 35 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Not stated

Sample collected by: Supervised patient/supervised parent

Sample collection method: Saliva (1 mL) was collected after the subjects had swilled their saliva around their mouths for at least 30 seconds and then spitting into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM).

Sample storage/transport: Minimum Essential Media (MEM)

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Migueres 2021 (f) (Continued)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: 2/303 (0.6%) saliva samples provided an indeterminate result.

Comparative

Notes

Funding: Hologic provided the molecular reagents for SARS-CoV-2 detection.

Publication status: Published paper

Source: Diagnostic Microbiology and Infectious Diseases

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Migueres 2021 (f) (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Miller 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and saliva samples for the diagnosis of COVID-19. Three different RNA extraction methods were compared, but only one was extracted for the purposes of this review. Design: 91 (36) symptomatic and asymptomatic adult participants referred by physicians at two primary care medicine facilities in NY Recruitment: Adult participants who had undergone assessment by RT-PCR within 5 days of study enrolment or were having a NP swab test at the time of enrolment Prospective or retrospective: Mixed prospective and retrospective

Miller 2020 (Continued)

	Exclusion criteria: Confirmed other respiratory infection, history of non-infectious disease such as vasculitis, dermatomyositis, idiopathic pulmonary fibrosis and organising pneumonia, less than 18 years, pregnancy
Patient characteristics and setting	Setting: Primary care Location: New York Country: USA Dates: Not stated Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: Healthcare worker/clinical trial co-ordinators Sample collection method: Swab; no details provided Sample storage/transport: VTM "Paired samples were transported at ambient temperature and tested within 48 hours after collection". Timing of sample collection: At or up to 5 days prior to healthcare visit (study enrolment) NAT extraction method: Manual method using the MagMAX Viral/Pathogen Nucleic Acid Isolation kit (ThermoFisher Scientific) Assay used: COVID-19 RT-PCR test (Phosphorus Diagnostics, LLC) Genetic target: N1, N2, Rnase P Threshold: Ct value, estimated as LOD based on spiked samples (Table 4) Blinding reported: Yes Threshold predefined: Yes Index Sample: Saliva Sample collection device: Orasure Oragene DX (OGD-510) device Sample collected by: Patient-supervised Sample collection method: Saliva, collected 'according to manufacturer's instructions' Sample storage/transport: "Paired samples were transported at ambient temperature and tested within 48 hours after collection". Timing of sample collection: At or up to 5 days prior to healthcare visit (study enrolment) NAT extraction method: As for reference sample Assay used: As for reference sample Genetic target: As for reference sample Threshold: As for sample A

Miller 2020 (Continued)

Blinding reported: Yes

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Simultaneous collection of paired samples

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Phosphorus Diagnostics, LLC

Publication status: Pre-print (not peer-reviewed)

Source: Preprint server (MedRxiv)

Author COI: COI declared: authors are shareholders and employees of Phosphorus Diagnostic, LLC, a commercial laboratory that provided SARS-CoV-2 testing

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	No		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Miller 2020 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes

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Miller 2020 (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Mora-Aguilera 2022 (a)
Study characteristics

Patient Sampling	Design: 2 x single cohorts (a) and (b) of ambulatory volunteers providing paired mouthwash and NPS samples because of 'suspected' COVID-19. Mixed symptomatic and asymptomatic (a third cohort comprising only mouthwash samples as a part of test development not extracted) Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 23 (9) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Unclear (including COVID-19 testing centre) Location: CDMX Cuauhtemoc District Country: Mexico Dates: March to June 2020 Symptoms and severity: 13/45 (28.9%) symptomatic Demographics: Age: Range: 19-81 Sex: 30/45 (66%) male (across Mora-Aguilera 2022 (a) and Mora-Aguilera 2022 (b)) Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swab Sample collection device: NS Sample collected by: NS (probably HCW) Sample collection method: Not stated Sample storage/transport: Not stated Timing of sample collection: Not stated NAT extraction method: Not stated Assay used: Not stated; quote: "The NPS specimens, collected on cohorts 2 and 3, were submitted to a blind national reference laboratory to perform the official test accepted by the World Health Organization (WHO)". Genetic target: Not stated Threshold: Not stated

Mora-Aguilera 2022 (a) (Continued)

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample: Sterile water gargle

Sample collection device: screw-cap plastic bottle

Sample collected by: Unsupervised patient

Sample collection method: MWS was vigorously stimulated with 1 mL of sterile distilled water for 40 s. Individuals were asked to avoid food eating and/or toothbrushing at least 1 h before sampling, keep the mouth closed during the MWS procedure to avoid aerosols [13–15], and stick the ID label and close the lid after collecting the total mouth fluids in a 100 mL sterile leak-proof, screw-cap plastic bottle containing 2 mL of lab-prepared viral Hanks's transport medium.

Sample storage/transport: 2 mL of lab-prepared viral Hanks's transport medium. Samples were stored at 4 °C/24 h

Timing of sample collection: NS

NAT extraction method: Manual RNA extraction: Hot acid phenol method and CTAB

Assay used: In-house RT-PCR protocol

Genetic target: N and RPP30 genes

Threshold: NS

Blinding reported: NS

Threshold predefined: Not stated

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Postgraduate College and Laboratory of Epidemiological Risk Analysis (LANREF)

Publication status: Published paper

Source: International Journal of Environmental Research and Public Health

Author COI: Authors declared no COI present.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Mora-Aguilera 2022 (a) *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
If a threshold was used, was it pre-specified?	Unclear
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	

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Mora-Aguilera 2022 (a) *(Continued)*
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Unclear

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Mora-Aguilera 2022 (b)
Study characteristics

Patient Sampling	Design: 2 x single cohorts (a) and (b) of ambulatory volunteers providing paired mouthwash and NPS samples because of 'suspected' COVID-19. Mixed symptomatic and asymptomatic (a third cohort comprising only mouthwash samples as a part of test development not extracted) Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 22 (4) Additional inclusion criteria: Cohort 1 only provided results of MWS samples.
Patient characteristics and setting	Setting: Unclear (including COVID-19 testing centre) Location: CDMX Cuauhtemoc District Country: Mexico Dates: March to June 2020 Symptoms and severity: 13/45 (28.9%) symptomatic Demographics: Age: Range: 19-81 Sex: 30/45 (66%) male

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Mora-Aguilera 2022 (b) (Continued)

(across [Mora-Aguilera 2022 \(a\)](#) and [Mora-Aguilera 2022 \(b\)](#))

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: NS

Sample collected by: NS (probably HCW)

Sample collection method: Not stated

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: Not stated; quote: "The NPS specimens, collected on cohorts 2 and 3, were submitted to a blind national reference laboratory to perform the official test accepted by the World Health Organization (WHO)".

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated

Index Sample: Sterile water gargle

Sample collection device: screw-cap plastic bottle

Sample collected by: Unsupervised patient

Sample collection method: MWS was vigorously stimulated with 1 mL of sterile distilled water for 40 s. Individuals were asked to avoid food eating and/or toothbrushing at least 1 h before sampling, keep the mouth closed during the MWS procedure to avoid aerosols [13–15], and stick the ID label and close the lid after collecting the total mouth fluids in a 100 mL sterile leak-proof, screw-cap plastic bottle containing 2 mL of lab-prepared viral Hanks's transport medium.

Sample storage/transport: 2 mL of lab-prepared viral Hanks's transport medium. Samples were stored at 4 °C/24 h.

Timing of sample collection: NS

NAT extraction method: Manual RNA extraction: Hot acid phenol method and CTAB

Assay used: In-house RT-PCR protocol

Genetic target: N and RPP30 genes

Threshold: NS

Blinding reported: NS

Threshold predefined: Not stated

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Mora-Aguilera 2022 (b) (Continued)

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Postgraduate College and Laboratory of Epidemiological Risk Analysis (LANREF)

Publication status: Published paper

Source: International Journal of Environmental Reserach and Public Health

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
If a threshold was used, was it pre-specified?	Unclear		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Mora-Aguilera 2022 (b) *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Moreno-Contreras 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between OP/NP and saliva samples for the diagnosis of COVID-19
	Design: 71 (34) primarily ambulatory symptomatic patients attending a respiratory triage centre

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Moreno-Contreras 2020 (Continued)

	Recruitment: Unclear Prospective or retrospective: Unclear Setting: Outpatient ambulatory triage except 3 samples collected from hospitalised patients
Patient characteristics and setting	Location: Tlaltenango Health Centre, Cuernavaca/Morelos Country: Mexico Dates: May 2 to May 31 Symptoms and severity: All patients had two or more symptoms related to COVID-19. No other details provided Demographics: Provided for total cohort of 253: Median age 41 years (± 14.4); Sex: 115 (45%) male Exposure history: Not stated
Index tests	Reference sample: Naso/oropharyngeal (NP/OP) Sample collected by: Not stated Sample collection method: Swab; no details provided Sample storage/transport: 2.5 mL of viral transportation medium. All samples were stored and kept at 4 °C until transported for analysis, which was within 24-36 hours after sample collection. Timing of sample collection: Median 4 days from symptom onset (range 1 to 7 days) NAT extraction method: QIAamp viral RNA mini kit (QIAGEN), following the manufacturer's protocol Assay used: StarQ One-step RT-qPCR (Genes 2 Life) kit Genetic target: Berlin Protocol: E gene and Rnase P Threshold: Ct value ≤ 38 Blinding reported: Not stated Threshold predefined: Yes Index Sample: Saliva Sample collected by: Patient Sample collection method: Saliva collected by repeatedly spitting into sterile urine collection cup and mixed with lysis buffer. Sample storage/transport: No VTM was added to the saliva samples. All samples were stored and kept at 4 °C until transported for analysis, which was within 24-36 hours after sample collection. Timing of sample collection: Median 4 days from symptom onset (range from 1 to 7 days) NAT extraction method: Quick Extract DNA Extraction Solution (QE, Lucigen) Assay used: As for reference sample

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Moreno-Contreras 2020 (Continued)

	Genetic target: As for reference sample		
	Threshold: As for reference sample		
	Blinding reported: Not stated		
	Threshold predefined: Yes		
Target condition and reference standard(s)			
Flow and timing	Sampling schedule prespecified: Yes Time interval between sampling methods: Paired samples; no further details provided All patients received all sampling methods: Yes Missing data: None reported Uninterpretable results: None reported Indeterminate results: None reported		
Comparative			
Notes	Funding: Consejo Nacional de Ciencia y Tecnología (CONACYT) Publication status: Pre-print (not peer-reviewed) Source: bioRxiv Author COI: No COI statement reported		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Moreno-Contreras 2020 *(Continued)*

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)

If a threshold was used, was it pre-specified?

Is undergoing one sample type unlikely to influence the result of the other sample type?

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Moreno-Contreras 2020 (Continued)

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Nacher 2021 (a)

Study characteristics

Patient Sampling

Design: Single group of persons aged 3 years and older with mild symptoms suggestive of COVID-19 and asymptomatic persons with a testing indication in French Guiana

Recruitment: Consecutive enrolment of those eligible and consenting

Prospective or retrospective: Prospective

Sample size (cases): 1028 (223)

Additional inclusion criteria: non-inclusion criteria included treatments that reduce salivary volume (anticholinergic activity) and impossibility of performing the nasopharyngeal swab.

Patient characteristics and setting

Setting: Mixed: hospital outpatients. Community and drive-through

Location: Cayenne Hospital, Red Cross mobile team

Country: French Guiana

Dates: July 22 to October 28, 2020

Symptoms and severity: 504/1028 (49%) asymptomatic

Demographics: 453/1028 (44%) males
Median age (IQR): 34 (23-47)

Exposure history: 277/1028 (26.9%) were contacts of cases.

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Healthcare workers

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Nacher 2021 (a) (Continued)

Sample collection method: Not stated

Sample storage/transport: Transport Medium nos: Samples were stored at 4 °C before analysis. Time until testing ranged from 0-100 hours.

Timing of sample collection: > 0-10 days after symptom onset

NAT extraction method: Qiasymphony system (QIAGEN, Hilden, Germany)

Assay used: GeneFinder COVID-19 Plus RealAmp kit (ELITechGroup, Puteaux, France)

Genetic target: RdRp, E and N genes

Threshold: A sample was considered positive if at least one of the RdRp, N or E genes were amplified with a Ct < 40.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Urine container; no details provided

Sample collected by: Unsupervised patient

Sample collection method: Patients were advised not to eat or drink and to rinse their mouth before the test; also to accumulate saliva in their mouth before spitting it in a dedicated container

Sample storage/transport: Dry/direct sampling. When saliva specimens presented high viscosity, they were fluidified with proteinase K using a 10% equivalent volume of the specimen, then vortexed and incubated at 56 °C during 15 minutes. If the collected volume of saliva was insufficient (< 1 mL), we completed up to 1 mL with NaCl 0.9% (192 samples (18.7%) were diluted with normal saline).

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: n = 56 saliva samples missing or spilt during transport; n = 11 NP samples missing or 'not analysed using study protocol'

Uninterpretable results: N = 6 saliva samples insufficient volume

Indeterminate results: None reported

Comparative

Notes

Funding: Ministère de l'Enseignement Supérieur et de la Recherche

Nacher 2021 (a) (Continued)

Publication status: Published paper

Source: PLoSOne

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			

Nacher 2021 (a) (Continued)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Nacher 2021 (b)

Study characteristics

Patient Sampling Design: Single group of persons aged 3 years and older with mild symptoms suggestive of COVID-19 and asymptomatic persons with a testing indication in French Guiana

Recruitment: Consecutive enrolment of those eligible and consenting

Prospective or retrospective: Prospective

Sample size (cases): 1028 (223)

Nacher 2021 (b) (Continued)

Additional inclusion criteria: non-inclusion criteria included treatments that reduce salivary volume (anticholinergic activity) and impossibility of performing the nasopharyngeal swab,

Patient characteristics and setting

Setting: Mixed: hospital outpatients. Community and drive-through

Location: Cayenne Hospital, Red Cross mobile team

Country: French Guiana

Dates: July 22 to October 28, 2020

Symptoms and severity: 504/1028 (49%) asymptomatic

Demographics: 453/1028 (44%) males

Median age (IQR): 34 (23-47)

Exposure history: 277/1028 (26.9%) were contacts of cases.

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Healthcare workers

Sample collection method: Not stated

Sample storage/transport: Transport Medium nos: Samples were stored at 4 °C before analysis. Time until testing ranged from 0-100 hours.

Timing of sample collection: > 0-10 days after symptom onset

NAT extraction method: Qiasymphony system (QIAGEN, Hilden, Germany)

Assay used: GeneFinder COVID-19 Plus RealAmp kit (ELITechGroup, Puteaux, France)

Genetic target: RdRp, E and N genes

Threshold: A sample was considered positive if at least one of the RdRp, N or E genes were amplified with a Ct < 40.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: Urine container; no details provided

Sample collected by: Unsupervised patient

Sample collection method: Patients were advised not to eat or drink and to rinse their mouth before the test; also to accumulate saliva in their mouth before spitting it in a dedicated container

Sample storage/transport: Dry/direct sampling. When saliva specimens presented high viscosity, they were fluidified with proteinase K using a 10% equivalent volume of the specimen, then vortexed and incubated at 56 °C during 15 minutes. If the collected volume of saliva was insufficient (< 1 mL), we completed up to 1 mL with NaCl 0.9% (192 samples (18.7%) were diluted with normal saline).

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Nacher 2021 (b) (Continued)

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: n = 56 saliva samples missing or spilt during transport; n = 11 NP samples missing or 'not analysed using study protocol'

Uninterpretable results: N = 6 saliva samples insufficient volume

Indeterminate results: None reported

Comparative

Notes

Funding: Ministère de l'Enseignement Supérieur et de la Recherche

Publication status: Published paper

Source: PLoS One

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			

Nacher 2021 (b) (Continued)

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias?

High risk

Otto 2020

Study characteristics

Patient Sampling

Single-group study to estimate agreement between NP and saliva samples for diagnosis of COVID-19

Design: 92 (49) outpatients with symptoms compatible with COVID-19 attending a COVID-19 consultation unit; none had a productive cough

Recruitment: Not stated

Prospective or retrospective: Prospective

Patient characteristics and setting

Setting: Outpatient COVID-19 unit

Location: Military Instruction Hospital Sainte Anne, Toulon

Country: France

Dates: April to September 2022

Symptoms and severity: All symptomatic

Demographics: Not reported

Exposure history: Not reported

Index tests

Reference Sample: Nasopharyngeal (NP)

Sample collected by: Experienced and trained physicians

Sample collection method: Not stated

Sample storage/transport: VTM used; immediately transferred to laboratory and inactivated with 10 µL of proteinase K (25 mg/mL) into 200 µL of specimen at 65°C during 10 minutes

Timing of sample collection: From 0 to >14 days pso

NAT extraction method: MagNA pure compact (Roche, Switzerland) or GenoXtract (Biocentric, France)

Assay used: RT-PCR; in-house (French National Center) protocol using a Light-Cycler 480 Real-Time PCR System (Roche, Switzerland)

Genetic target: RdRp (IP2 and IP4 regions)

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva

Sample collected by: Patient

Sample collection method: Patients asked to cough keeping their surgical mask on, and then collect saliva themselves into a sterile container.

Sample storage/transport: No VTM used; immediately transferred to laboratory and inactivated with 10 µL of proteinase K (25 mg/mL) into 200 µL of specimen at 65°C during 10 minutes

Timing of sample collection: From 0 to > 14 days pso

Otto 2020 (Continued)

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes, single collection

Time interval between sampling methods: Apparently simultaneous

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Supported by Service de Santé des Armées (France).

Publication status: Published

Source: Clinical Infectious Diseases

Author COI: Authors reported no COI.

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Was a case-control design avoided?

Yes

Did the study avoid inappropriate exclusions?

Unclear

Did the study avoid inappropriate inclusions?

Yes

Was the intention that patients receive all tests at all time points?

Yes

Could the selection of patients have introduced bias?

Unclear risk

Are there concerns that the included patients and setting do not match the review question?

Low concern

Otto 2020 (Continued)

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard
Could the reference standard, its conduct, or its interpretation have introduced bias?
Are there concerns that the target condition as defined by the reference standard does not match the question?
DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes

Otto 2020 (Continued)

Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Pasomsub 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP/OP and saliva samples for the diagnosis of COVID-19 Design: 200 (21) symptomatic adults who either had a history of recent high risk travel or close contact with a COVID-19 case attending an acute respiratory infection clinic Recruitment: Unclear. Prospective or retrospective: Prospective Inclusion criteria: History of fever or acute respiratory symptoms together with (a) a travel history of COVID-19 within 14 days or, (b) history of contact with an individual who was confirmed to have or suspected or having COVID-19. Exclusion criteria: < 18 years
Patient characteristics and setting	Setting: Hospital outpatient Location: Ramathibodi Hospital, Bangkok, Thailand Country: Thailand Dates: Between 27 March and 4 April Symptoms and severity: Symptoms at presentation for all patients Cough: 108/200 (54%) Sore throat: 102/200 (51%) Runny nose: 68/200 (34%) Sneezing: 26/200 (13%) Dyspnoea: 73/200 (37%) Demographics: Age median: 36 IQR (28-48) Sex: 69/200 (35%) male Exposure history: Close contact COVID-19 case 170/200 (85%)
Index tests	Reference Sample: Naso/oropharyngeal (NP/OP) Sample collected by: Not stated Sample collection method: COPAN FLOQS-swabs into sterile tube Sample storage/transport: Copan's Universal Transport Medium (UTM) Viral RNA extracted from samples within 26 minutes of collection. Timing of sample collection: Median 3 days IQR (2-7) pso

Pasomsu 2020 (Continued)

NAT extraction method: Viral RNA was extracted from 200 mL of the samples within 26 minutes using MagDEA® Dx reagents (Precision System Science, Chiba, Japan). Following the manufacturer's instructions

Assay used: Diagnostic Kit (Sansure, Changsha, China)

Genetic target: ORF1ab and N gene fragments

Threshold: (Ct) values of both target genes ≤ 38

Retesting of samples with discordant gene Ct values. Specimens repeatedly discordant were reported as negative.

Blinding reported: Yes.

Threshold predefined: Yes

Index Sample: Saliva

Sample collected by: Not stated

Sample collection method: Sputum collection container containing Copan's Universal Transport Medium (UTM)

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Yes

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Before collecting NP/throat swabs, individuals were asked to collect the saliva samples.

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: This study was supported by a grant from the Faculty of Medicine Ramathibodi Hospital, Mahidol University.

Publication status: Published paper

Source: Academic Journal

Author COI: All authors declared that there were no conflicts of interest.

Methodological quality

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Pasomsb 2020 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Pasomsb 2020 (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Patel 2020

Study characteristics

Patient Sampling	Single-group study to compare agreement between OP and NP swabs for detection of COVID-19 Design: 146 (25) individuals $\leq$ 7 days post-'illness onset' Recruitment: Unclear. Assumed convenience sample of paired samples sent to CDC Prospective or retrospective: Retrospective
Patient characteristics and setting	Setting: Not stated Location: Centres for Disease Control and Prevention Country: United States Dates: January 27, 2020–February 29, 2020 Symptoms and severity: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Patel 2020 (Continued)

Demographics: Median age 40 years IQR (24-56)
Sex: 81/146 (56%) male
Exposure history: Not stated

Index tests

Reference Sample: Nasopharyngeal (NP)

Sample collected by: Not stated

Sample collection method: Swab nos

Sample storage/transport: Not stated

Timing of sample collection: Median of 2 days (interquartile range [IQR]: 1-4 days) pso

NAT extraction method: Not stated

Assay used: CDC 2019-Novel Coronavirus (nCoV) Real-Time Reverse Transcriptase (RT)-Polymerase Chain Reaction (PCR) Diagnostic Panel

Genetic target: N1, N2,N3 Nucleocapsid gene regions

Threshold: A positive CDC 2019-nCoV RT-PCR Diagnostic Panel test was defined by a cycle threshold (Ct) value of < 40 for all three gene regions.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Oropharyngeal (OP)

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: Swab nos

Sample storage/transport: Not stated

Timing of sample collection: As for sample A

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Swabs collected on the same date on the same person (within 24 hours)

All patients received all sampling methods: Not stated

Missing data: None reported

Uninterpretable results: None reported

Patel 2020 (Continued)

Indeterminate results: None reported

Comparative

Notes

Funding: No external funding was received.

Publication status: Published accepted manuscript

Source: Academic Journal

Author COI: All authors reported no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		

Patel 2020 (Continued)

Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Collection method)		
DOMAIN 2: Index test (Oropharyngeal/nasal)		
DOMAIN 2: Index test (Nasal)		
DOMAIN 2: Index test (Oral rinse)		
DOMAIN 2: Index test (Operator)		
DOMAIN 3: Reference standard		
Could the reference standard, its conduct, or its interpretation have introduced bias?		
Are there concerns that the target condition as defined by the reference standard does not match the question?		
DOMAIN 4: Flow and timing		
Was there an appropriate interval between index tests?	Yes	
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes	
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes	
Were results presented per patient?	Yes	
Were all patients included in the analysis?	Unclear	
Could the patient flow have introduced bias?		Unclear risk

Patriquin 2022

Study characteristics

Patient Sampling	Design: Single group of adults recruited from two dedicated COVID-19 testing centres during a four-day period in January 2022, meeting eligibility criteria for molecular diagnostic testing by Public Health: Symptomatic or close contact AND - 50 years and over - Unvaccinated - Live or work in congregate settings e.g. residential care, shelters, corrections - HCW

Patriquin 2022 (Continued)

- Adults 18-49 with risk factors for severe disease
- Children < 18 with risk factors for severe disease
- Pregnant
- African ethnicity

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): 392 (64)

Additional inclusion criteria: None

Patient characteristics and setting

Setting: COVID-19 testing centre/drive-through

Location: Public Health Mobile Testing Unit and Urban-based COVID-19 testing centres, Nova Scotia

Country: Canada

Dates: January 2022

Symptoms and severity: Most participants symptomatic or close contacts of a known case

Demographics: All participants were adults

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Flocked swab (Copan Diagnostics, Inc., (Murrietta, CA), or AccuViral Collection Kit, (AccuGene, San Diego, CA))

Sample collected by: Not stated. Probably HCW

Sample collection method: Standardised sampling technique with a flocked swab. Collected before OP/nasal anterior nares

Sample storage/transport: VTM. Samples refrigerated at 4 °Celsius. Samples were immediately transported to a central laboratory and NAAT was performed within 12 h according to manufacturer instructions.

Timing of sample collection: NS

NAT extraction method: NS

Assay used: Samples were initially tested by the Aptima SARS-CoV-2 Assay on the Panther System (Hologic Inc., San Diego, CA); negative results were confirmed by the Cobas 6800 instrument (Roche Diagnostics, Rotkreuz, 74 Switzerland) and positive results by both the Roche 6800 assay and the Xpert Xpress SARS-CoV-2 test 76 (Cepheid, Sunnyvale, CA).

Genetic target: Not stated

Threshold: A positive swab result was defined as SARS-CoV-2 detection in at least two NAATs.

A positive diagnosis was defined as an individual being positive on any one swab.

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Oropharyngeal/nasal anterior nares swab

Patriquin 2022 (Continued)

Sample collection device: LASSIQSwab fiber-tip swab from Copan Italia (Brescia, Italy)

Sample collected by: Not stated. Probably HCW

Sample collection method: According to a 'previously described' collection technique. Collected after NPS

Sample storage/transport: VTM

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Preprint

Source: MedRxiv

Author COI: No COI statement reported

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Was a case-control design avoided?

Yes

Did the study avoid inappropriate exclusions?

Unclear

Did the study avoid inappropriate inclusions?

Unclear

Was the intention that patients receive all tests at all time points?

Unclear

Patriquin 2022 (Continued)

Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	No
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	

Patriquin 2022 *(Continued)*

Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Pere 2020

Study characteristics	
Patient Sampling	Single-group study to agreement between NP and nasal swabs Design: 44 (37) patients suspected of COVID-19 selected for testing according to medical decision Recruitment: Not stated Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Unclear; participants 'attending' a hospital Location: Hôpital Européen Georges Pompidou, Paris Country: France Dates: Not stated; 'up to the end of March 2020' Symptoms and severity: Not stated Demographics: Median age: 63 years IQR (18-94) Sex: 23/44 (53%) male Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: Not stated Sample collection method: Sample collection device: Xpert nasopharyngeal sample collection kit, Cepheid, Sunnyvale, CA, USA Swab inserted in the nostril to the back of the nasopharyngeal cavity, rotated five times, and removed Sample storage/transport: Vial containing 3 mL of virus transport medium (Xpert viral transport medium; Cepheid)

Pere 2020 (Continued)

Timing of sample collection: Not stated; patients 'attending' hospital

NAT extraction method: Not stated

Assay used: Allplex 2019-nCoV assay (Seegene, Seoul, Korea)

Genetic target: Not stated

Threshold: Not stated; appears to be < 40 Ct

Blinding reported: Not stated

Threshold predefined: Not stated; presume as per manufacturer

Index Sample: Nasal

Sample collected by: Not stated

Sample collection method: Sample collection device: Copan Transystem, Brescia, Italy. Swab inserted in a single nostril to the inferior concha, rotated five times, and removed

Sample storage/transport: 15 mL tube containing 3 mL of saline solution (0.9% NaCl)

Timing of sample collection: Not stated; patients 'attending' hospital

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: Appears to be as for reference sample

Blinding reported: Not stated

Threshold predefined: Not stated; presume as per manufacturer

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Not stated

Time interval between sampling methods: Simultaneous; paired samples

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement reported

Publication status: Published

Source: Journal of Clinical Microbiology

Author COI: No COI statement reported

Methodological quality

Pere 2020 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern

Pere 2020 (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Pham 2020

Study characteristics

Patient Sampling	Single-group study to validate a new NAAT in comparison to an EUA RT-PCR assay, and to compare agreement between NP, OP and nasal samples for the diagnosis of COVID-19 <i>Only EUA RT-PCR assay extracted for this review</i> Design: 35 (14) symptomatic patients suspected of being infected with SARS-CoV-2 and with three different sample types available (NP, OP, and nasal swabs) Recruitment: Unclear Prospective or retrospective: Unclear
Patient characteristics and setting	Setting: Unclear Location: Two clinical sites mentioned. Author institutions include Scripps Health, San Diego, CA and Montefiore Medical Center, Bronx NY. Country: United States

Pham 2020 (Continued)

Dates: Not reported

Symptoms and severity: All symptomatic

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference Sample: Nasopharyngeal (NP)

Sample collected by: Not stated.

Sample collection method: Not described. Sample collection device: Copan Minitip flocced swab and VTM

Sample storage/transport: Samples stored in VTM, frozen and shipped to Hologic

Timing of sample collection: Not stated

NAT extraction method: Automated, as part of NAT

Assay used: Hologic Panther Fusion SARS-CoV-2 RT-PCR EUA assay

Genetic target: Not stated

Threshold: Not reported; highest reported Ct value was 35.3

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample [A]: Oropharyngeal (OP)

Sample collected by: Not stated

Sample collection method: Swab the posterior pharynx for 3-5 seconds and place swab into a specimen tub

Sample storage/transport: Samples stored in Hologic Aptima Specimen Transport Medium (STM), frozen and shipped to Hologic

Timing of sample collection: Not stated

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample [B]: Nasal

Sample collected by: Not stated

Sample collection method: Insert swab into the subject's nostril past in the inferior turbinate, approximately 3 cm, twisting the swab in mid-turbinate area for 3 to 5 seconds and placing the swab into a tube

Sample storage/transport: Samples stored in Hologic Aptima Specimen Transport Medium (STM), frozen and shipped to Hologic

Timing of sample collection: Not stated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Pham 2020 (Continued)

	NAT extraction method: As for reference sample
	Assay used: As for reference sample
	Genetic target: As for reference sample
	Threshold: As for reference sample
	Blinding reported: Not stated
	Threshold predefined: Yes
Target condition and reference standard(s)	
Flow and timing	Sampling schedule prespecified: Not stated Time interval between sampling methods: Unclear. NP swabs described, then stated nasal swabs 'were collected first ... OP samples were collected immediately following nasal samples'. All patients received all sampling methods: Yes Missing data: Unclear. 140 symptomatic patients provided NP swabs and 'an additional clinical sample set ... of paired ... specimens were collected'; not clear why only a subgroup with paired specimens Uninterpretable results: None reported Indeterminate results: None reported
Comparative	
Notes	Funding: The study was funded by Hologic Inc. Publication status: Accepted manuscript Source: Journal of Clinical Microbiology Author COI: All authors except I. McHardy, I. Gendlina, D.Y. Goldstein, and A.S. Fox are scientists employed by Hologic Inc., the manufacturer of the diagnostic test systems used in this study. IM, IG, DYG and ASF declared no conflicts of interest.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		

Pham 2020 (Continued)

Could the selection of patients have introduced bias?		Unclear risk
Are there concerns that the included patients and setting do not match the review question?		Unclear
DOMAIN 2: Index test (Saliva)		
DOMAIN 2: Index test (Gargle)		
DOMAIN 2: Index test (Oral swab)		
DOMAIN 2: Index test (Oropharyngeal)		
If a threshold was used, was it pre-specified?	Yes	
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear	
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear	
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear	
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Collection method)		
DOMAIN 2: Index test (Oropharyngeal/nasal)		
DOMAIN 2: Index test (Nasal)		
If a threshold was used, was it pre-specified?	Yes	
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear	
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear	
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear	
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk

Pham 2020 (Continued)

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? No

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Potter 2022
Study characteristics

Patient Sampling	Design: [1] Single group of symptomatic healthcare personnel with COVID-19-compatible symptoms and symptomatic patients who met clinical criteria for SARS-CoV-2 and presented to the Emergency Department tested with the Lyra SARS-CoV-2
Patient characteristics and setting	Setting: Mixed (COVID-19 testing centre (HCW) AND Emergency Department (patients)) Location: Barnes-Jewish Hospital/Washington University Medical Center Country: USA Dates: April 27 to May 20, 2020 Symptoms and severity: All subjects included were symptomatic at testing time Demographics: Not stated

Potter 2022 (Continued)

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Healthcare worker

Sample collection method: A flocked NP swab was collected as part of standard of care and placed into universal transport medium or ESwab liquid Amies transport medium.

Sample storage/transport: UTM or Eswab liquid Amies transport medium. The 50 mL conical tube was transported to the laboratory with the NP swab specimen. The tubes were vortexed for 10 s, and frozen at 80 °C until analysis. The remnant universal transport medium from the NP swab was also frozen at 80 °C and was analysed concurrently with the saliva specimen.

Timing of sample collection: NS

NAT extraction method: NUCLISENS-easyMAG automated extraction system

Assay used: Quidel Lyra SARS-CoV-2 assay (Lyra)

Genetic target: pp1ab target gene

Threshold: Not stated

Blinding reported: NS

Threshold predefined: Not stated

Index Sample: Saliva spit

Sample collection device: Nunc 50 mL conical (Thermo Fisher Scientific), CellPro 50 mL conical (Alkali Scientific), or Corning Self Standing 50 mL conical (Corning) tubes

Sample collected by: Unsupervised patient

Sample collection method: A small amount of saliva (approximately 1 mL) should be placed in a 50 mL conical tube, put into a plastic bag, and given to the HCP collecting the NP swab. Patients were instructed to “spit” into a 50 mL conical tube. No specific exclusions related to food/drink consumption prior to specimen collection were provided to either cohort.

Sample storage/transport: Dry/direct sampling. PBS was added. The 50 mL conical tube was transported to the laboratory with the NP swab specimen.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

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Potter 2022 (Continued)

Missing data: 231/542 samples not included in main analysis because participants were not able to produce enough saliva

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Not stated

Publication status: Published paper

Source: Journal of Applied Laboratory Medicine

Author COI: N.W. Anderson is a member of the Diasorin Molecular Scientific advisory board. C.-A.D. Burnham, Cepheid. Honoraria: C.-A.D. Burnham, BioFire, Roche. Research Funding: J.H. Kwon is supported by the grant 1K23AI137321-01A1 from the National Institute of Allergy and Infectious Diseases. C.-A.D. Burnham, grants from Cepheid, bioMerieux, Luminex, and BioFire to institution

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?	Unclear		

Was a case-control design avoided?	Yes		

Did the study avoid inappropriate exclusions?	Unclear		

Did the study avoid inappropriate inclusions?	Unclear		

Was the intention that patients receive all tests at all time points?	Unclear		

Could the selection of patients have introduced bias?		Unclear risk	

Are there concerns that the included patients and setting do not match the review question?			Unclear

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified?	Unclear		

Is undergoing one sample type unlikely to influence the result of the other sample type?	No		

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		

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Potter 2022 (Continued)

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear

Potter 2022 (Continued)

Could the patient flow have introduced bias?

High risk

Procop 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and saliva samples for the diagnosis of COVID-19 Design: 224 (42) patients with symptoms consistent with COVID-19 (determined by a licensed healthcare provider and reviewed by a second healthcare provider) attending drive-through specimen collection unit Recruitment: Not stated Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: COVID-19 testing clinic (drive-through) Location: Not stated; author institution Cleveland Clinic, Cleveland, Ohio Country: USA Dates: Not stated Symptoms and severity: All symptomatic. No further details Demographics: Mean age 44 y (18-82 y) Sex: 14 (36%) male; ethnicity included black (19, 49%), white (13, 33%), multiracial (3, 8%), Hispanic (1), other (1), declined (1), unavailable (1) Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: trained healthcare professional Sample collection method: Not stated Sample storage/transport: placed in 0.9% normal saline; refrigerated at the collection site and transported to the laboratory in insulated coolers with ice packs. All samples tested on day of collection Timing of sample collection: Not stated NAAT extraction method: MagNA Pure system (Roche Diagnostics, Indianapolis, IN); 200 µl specimen was rendered non-infectious using bacterial lysis buffer (Roche Diagnostics, Indianapolis, IN). Then, 200 µl inactivated specimen processed for extraction Assay used: RT-PCR; CDC 2019 nCoV real-time RT-PCR diagnostic panel (4 February 2020 version) using ABI 7500 Fast Dx instruments Genetic target: N gene (3 targets) plus RNaseP control Threshold: All 3 targets required for test positive; indeterminate if < 3 targets amplified (excluded but reported separately); negative if no N gene targets plus RNase P detected; test failure if no N gene targets and no amplification of the RNase P gene target Blinding reported: Not stated

Procop 2020 (Continued)

Threshold predefined: Yes

Index Sample: Saliva

Sample collected by: patient

Sample collection method: patient instructed to sniff strongly to gather any nasal secretion/mucus into the oropharynx, to cough to produce any phlegm, and then to submit these secretions and additional saliva until the specimen reached the premarked fill line: *3 mL requested but any accepted
Collected into a sterile container (urine cup)

Sample storage/transport: No VTM used; prior to testing, viscous samples were rendered more liquid using 0.5% dithiothreitol. All samples tested on day of collection

Timing of sample collection: Not stated.

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Simultaneous; enhanced saliva before NP

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: 1; no amplification of any N gene target or Rnase P control

Indeterminate results: NP: 2 indeterminate (1 or 2 targets amplified), both saliva +ve
Saliva: 5 indeterminate, 4 NP -ve (all with only 1 of 3 targets amplified for saliva) and 1 NP +ve (2 of 3 targets amplified for saliva)

Comparative

Notes

Funding: No funding statement provided

Publication status: Published

Source: Journal of Clinical Microbiology

Author COI: No COI statement provided

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Procop 2020 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	

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Procop 2020 (Continued)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Rajh 2021[A]

Study characteristics

Patient Sampling

Design: [1] Single group of symptomatic and asymptomatic individuals from a public COVID-19 testing site
[2] Group of 79 hospitalised COVID-19 patients (population pre-selected- not extracted for this review)
[3] Group of 750 individuals with no signs of infection and healthcare workers (not extracted for this review)

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): Total by saliva collection method:
a) Oral Rayon swab = 85 (34); b) Oral Nylon swab = 500 (147); c) Saliva drool = 190 (104)

Rajh 2021[A] (Continued)

Additional inclusion criteria: Unclear if sample 3 was useful (repeated samples, unclear verification of negative results)
RT-LAMP results compared to RT-PCR NP results (different technologies, not eligible for this review)

Patient characteristics and setting

Setting: COVID-19 testing centre
Location: Emergency Medical Service, Jesenice
Country: Slovenia
Dates: Not stated
Symptoms and severity: Not stated
Demographics: Not stated
Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab
Sample collection device: Not stated
Sample collected by: HCW
Sample collection method: NS
Sample storage/transport: VTM. 'Subject to routine testing on the same day' as collection
Timing of sample collection: NS
NAT extraction method: QIAcube Connect (QIAGEN, Germantown, MD, USA) and QIAamp Viral RNA Mini Kit (QIAGEN, Germantown, MD, USA)
Assay used: LDT PCR using RGQ PCR cyclers (QIAGEN, Germantown, MD, USA)
Genetic target: E and RdRP genes
Threshold: Samples with Cq < 38 were considered positive
Blinding reported: NS
Threshold predefined: Yes
Index Sample (A): Oral swab nos/Rayon
Sample collection device: Not stated
Sample collected by: Unsupervised patient
'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.'
Sample collection method: Rayon-tipped swab (155C, Copan Italy, Brescia, Italy)
Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing
Timing of sample collection: NS
NAT extraction method: No RNA extraction; saliva samples were heat-treated.
Assay used: LDT PCR using Light Cycler 480 Real-Time
PCR System (S-5/20 protocol)

Rajh 2021[A] (Continued)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Oral swab nos/Nylon

Sample collection device: Not stated

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.'

Sample collection method: FLOQ Swabs, regular moulded nylon swab (520CS01, Copan Italy, Brescia, Italy)

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Assay used: LDT PCR using Light Cycler 480 Real-Time

PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Index Sample (C): Saliva drool

Sample collection device: Microcentrifuge tubes; no other details provided

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.'

Sample collection method: Microcentrifuge tubes with 100 L of the RNA stabilisation buffer

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Assay used: LDT PCR using Light Cycler 480 Real-Time PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Rajh 2021[A] (Continued)

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Slovenian Research Agency (ARRS)

Publication status: Published paper

Source: Molecules

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
If a threshold was used, was it pre-specified?	Yes		

Rajh 2021[A] (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Unclear
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples,	Yes

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Rajh 2021[A] (Continued)

different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)?

Unclear

Were results presented per patient?

Yes

Were all patients included in the analysis?

Unclear

Could the patient flow have introduced bias?

Unclear risk

Rajh 2021[B]

Study characteristics

Patient Sampling

Design: [1] Single group of symptomatic and asymptomatic individuals from a public COVID-19 testing site
[2] Group of 79 hospitalised COVID-19 patients (population pre-selected- not extracted for this review)
[3] Group of 750 individuals with no signs of infection and healthcare workers (not extracted for this review)

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): Total by saliva collection method:

a) Oral Rayon swab = 85 (34); b) Oral Nylon swab = 500 (147); c) Saliva drool = 190 (104)

Additional inclusion criteria: Unclear if sample 3 was useful (repeated samples, unclear verification of negative results)

RT-LAMP results compared to RT-PCR NP results (different technologies, not eligible for this review)

Patient characteristics and setting

Setting: COVID-19 testing centre

Location: Emergency Medical Service, Jesenice

Country: Slovenia

Dates: Not stated

Symptoms and severity: Not stated

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: NS

Rajh 2021[B] (Continued)

Sample storage/transport: VTM. 'Subject to routine testing on the same day' as collection

Timing of sample collection: NS

NAT extraction method: QIAcube Connect (QIAGEN, Germantown, MD, USA) and QIAamp Viral RNA Mini Kit (QIAGEN, Germantown, MD, USA)

Assay used: LDT PCR using RGQ PCR cycler (QIAGEN, Germantown, MD, USA)

Genetic target: E and RdRP genes

Threshold: Samples with Cq < 38 were considered positive.

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Oral swab nos/Rayon

Sample collection device: Not stated

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.

Sample collection method: Rayon-tipped swab (155C, Copan Italy, Brescia, Italy)

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Assay used: LDT PCR using Light Cyclor 480 Real-Time

PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Oral swab nos/Nylon

Sample collection device: Not stated

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.

Sample collection method: FLOQ Swabs, regular moulded nylon swab (520CS01, Copan Italy, Brescia, Italy)

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Assay used: LDT PCR using Light Cyclor 480 Real-Time

Rajh 2021[B] (Continued)

PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Index Sample (C): Saliva drool

Sample collection device: Microcentrifuge tubes; no other details provided

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.

Sample collection method: Microcentrifuge tubes with 100 L of the RNA stabilisation buffer

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Assay used: LDT PCR using Light Cycler 480 Real-Time PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Slovenian Research Agency (ARRS)

Publication status: Published paper

Source: Molecules

Author COI: Authors declared no COI.

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

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Rajh 2021[B] (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Unclear
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oropharyngeal)	

Rajh 2021[B] (Continued)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Unclear

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Rajh 2021[C]

Study characteristics

Patient Sampling	Design: [1] Single group of symptomatic and asymptomatic individuals from a public COVID-19 testing site [2] Group of 79 hospitalised COVID-19 patients (population pre-selected- not extracted for this review)

Rajh 2021[C] (Continued)

[3] Group of 750 individuals with no signs of infection and healthcare workers (not extracted for this review)

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): Total by saliva collection method:

a) Oral Rayon swab = 85 (34); b) Oral Nylon swab = 500 (147); c) Saliva drool = 190 (104)

Additional inclusion criteria: Unclear if sample 3 was useful (repeated samples, unclear verification of negative results)

RT-LAMP results compared to RT-PCR NP results (different technologies, not eligible for this review)

Patient characteristics and setting

Setting: COVID-19 testing centre

Location: Emergency Medical Service, Jesenice

Country: Slovenia

Dates: Not stated

Symptoms and severity: Not stated

Demographics: Not stated

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: HCW

Sample collection method: NS

Sample storage/transport: VTM. 'Subject to routine testing on the same day' as collection

Timing of sample collection: NS

NAT extraction method: QIAcube Connect (QIAGEN, Germantown, MD, USA) and QIAamp Viral RNA Mini Kit (QIAGEN, Germantown, MD, USA)

Assay used: LDT PCR using RGQ PCR cycler (QIAGEN, Germantown, MD, USA)

Genetic target: E and RdRp genes

Threshold: Samples with Cq < 38 were considered positive.

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Oral swab nos/Rayon

Sample collection device: Not stated

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.

Sample collection method: Rayon-tipped swab (155C, Copan Italy, Brescia, Italy)

Rajh 2021[C] (Continued)

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Assay used: LDT PCR using Light Cycler 480 Real-Time

PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Oral swab nos/Nylon

Sample collection device: Not stated

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.

Sample collection method: FLOQ Swabs, regular moulded nylon swab (520CS01, Copan Italy, Brescia, Italy)

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Assay used: LDT PCR using Light Cycler 480 Real-Time

PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Index Sample (C): Saliva drool

Sample collection device: Microcentrifuge tubes; no other details provided

Sample collected by: Unsupervised patient

'We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 L and after collection, tube should be refrigerated.

Sample collection method: Microcentrifuge tubes with 100 L of the RNA stabilisation buffer

Sample storage/transport: RNA stabilisation fluid. Cooled on ice and frozen at -80 °C until further processing

Timing of sample collection: NS

NAT extraction method: No RNA extraction; saliva samples were heat-treated.

Rajh 2021[C] (Continued)

Assay used: LDT PCR using Light Cycler 480 Real-Time PCR System (S-5/20 protocol)

Genetic target: N2 and N2 genes

Threshold: Cq values of < 40 for N1 and N2

Blinding reported: NS

Threshold predefined: Yes

Target condition and reference
standard(s)

Flow and timing

Simultaneous sample collection: Unclear

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Slovenian Research Agency (ARRS)

Publication status: Published paper

Source: Molecules

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random
sample of patients enrolled?

Unclear

Was a case-control design avoid-
ed?

Unclear

Did the study avoid inappropriate
exclusions?

Unclear

Did the study avoid inappropriate
inclusions?

Unclear

Was the intention that patients
receive all tests at all time points?

Unclear

**Could the selection of patients
have introduced bias?**

Unclear risk

**Are there concerns that the in-
cluded patients and setting do
not match the review question?**

Unclear

DOMAIN 2: Index test (Saliva)

Rajh 2021[C] (Continued)

If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	

Rajh 2021[C] (Continued)

Was there an appropriate interval between index tests?	Unclear
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Unclear
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Rao 2021(a)

Study characteristics

Patient Sampling	Design: Single group of asymptomatic participants undergoing surveillance testing at Pokok Sena detention centre Recruitment: Unclear: "A cross-sectional two cohort diagnostic study was conducted on candidates who were undergoing surveillance testing for SARS-CoV-2 (...) and among asymptomatic travelers arriving at Kuala Lumpur International Airport (KLIA) throughout the month of September 2020". Random participants were asked to provide a deep throat saliva specimen prior to a routine OP/NP sample. Prospective or retrospective: Unclear Sample size (cases): 210 (59) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Other: Detention centre Location: Pokok Sena detection center at Kota Setar District, Kedah Country: Malaysia Dates: October 3 to October 10, 2020 Symptoms and severity: All participants were asymptomatic at the time of testing. Demographics: Median age 33 (IQR: 25-42) Gender, male: 392 (69.8%) (across Rao 2021 (b) and Rao 2021(a)) Exposure history: Not stated

Rao 2021(a) (Continued)

Index tests

Reference sample: Mixed NP/OP

Sample collection device: Not stated

Sample collected by: Not stated

Sample collection method: Samples collected using sterile flocked swabs and placed in a sterile tube containing viral transport medium (VTM)

Sample storage/transport: VTM. Samples kept in a cold room for approximately 1–2 h before being transferred to a central laboratory, within 6–9 h. Samples were processed and analysed within 48 h upon arrival at the research laboratory.

Timing of sample collection: NS

NAT extraction method: Magna Pure 96 DNA and Viral NA Small Volume extraction kit (Roche Diagnostic GmbH)

Assay used: one-step RT-PCR of a DiaPlexQ™Novel Coronavirus (2019-nCoV) Detection Kit (Solgent Co., Ltd.)

Genetic target: N and ORF1a genes

Threshold: Samples were classified as positive for SARS-CoV-2 when either one or both gene primer-probe sets were detected at a Ct value of < 40 as per kit's instructions.

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Deep throat/oropharyngeal saliva

Sample collection device: Sterile collection container; no more details provided

Sample collected by: Patients self-collected; no more details provided

Sample collection method: Candidates were instructed to avoid food and water for 1 h during the collection of 2 mL of deep throat saliva.

Sample storage/transport: Direct sampling

Timing of sample collection: As for the reference standard sample

NAT extraction method: As for the reference standard sample

Assay used: As for the reference standard sample

Genetic target: As for the reference standard sample

Threshold: As for the reference standard sample

Blinding reported: As for the reference standard sample

Threshold predefined: As for the reference standard sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Rao 2021(a) (Continued)

Comparative

Notes

Funding: Ministry of Health Malaysia Research Grant

Publication status: Published paper

Source: Journal of Medical Virology

Author COI: Authors declared no COI.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	No		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	No		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern

Rao 2021(a) (Continued)

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Rao 2021 (b)

Study characteristics

Patient Sampling	Design: Single group of asymptomatic travellers arriving at Kuala Lumpur International airport
	Recruitment: Unclear: "A cross-sectional two cohort diagnostic study was conducted on candidates who were undergoing surveillance testing for SARS-CoV-2 (...) and

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Rao 2021 (b) (Continued)

	among asymptomatic travelers arriving at Kuala Lumpur International Airport (KLIA) throughout the month of September 2020". Random participants were asked to provide a deep throat saliva specimen prior to a routine OP/NP sample. Prospective or retrospective: Unclear Sample size (cases): 351 (5) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Other: Airport Location: Kuala Lumpur International Airport Country: Malaysia Dates: October 3 to October 10, 2020 Symptoms and severity: All participants were asymptomatic at the time of testing. Demographics: Median age 33 (IQR: 25-42) Gender, male: 392 (69.8%) (across Rao 2021 (b) and Rao 2021(a)) Exposure history: Not stated
Index tests	Reference sample: Mixed NP/OP Sample collection device: Not stated Sample collected by: Not stated Sample collection method: Samples collected using sterile flocked swabs and placed in a sterile tube containing viral transport medium (VTM) Sample storage/transport: VTM. Samples transferred to the central laboratory directly within 3–4 h. Samples were processed and analysed within 48 h upon arrival at the research laboratory. Timing of sample collection: NS NAT extraction method: Magna Pure 96 DNA and Viral NA Small Volume extraction kit (Roche Diagnostic GmbH) Assay used: one-step RT-PCR of a DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit (Solgent Co., Ltd.) Genetic target: N and ORF1a genes Threshold: Samples were classified as positive for SARS-CoV-2 when either one or both gene primer-probe sets were detected at a Ct value of < 40 as per kit's instructions. Blinding reported: NS Threshold predefined: NS Index Sample: Deep throat/oropharyngeal saliva Sample collection device: Sterile collection container; no more details provided Sample collected by: Patients self-collected; no more details provided Sample collection method: Candidates were instructed to avoid food and water for 1 h during the collection of 2 mL of deep throat saliva.

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Rao 2021 (b) (Continued)

AS 2022 (2) (continued)

	Sample storage/transport: Direct sampling
	Timing of sample collection: As for the reference standard sample
	NAT extraction method: As for the reference standard sample
	Assay used: As for the reference standard sample
	Genetic target: As for the reference standard sample
	Threshold: As for the reference standard sample
	Blinding reported: As for the reference standard sample
	Threshold predefined: As for the reference standard sample
Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: None reported Uninterpretable results: None reported Indeterminate results: None reported
Comparative	
Notes	Funding: Ministry of Health Malaysia Research Grant Publication status: Published paper Source: Journal of Medical Virology Author COI: Authors declared no COI.
Methodological quality	
Item	Authors' judgement
DOMAIN 1: Patient selection	
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear

Rao 2021 (b) (Continued)

DOMAIN 2: Index test (Saliva)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? No

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? No

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients re-

Rao 2021 (b) (Continued)

ceive all index tests (samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Sahajpal 2021

Study characteristics

Patient Sampling	Design: Unclear group of 240 samples, 95 from a healthcare setting and 145 from a community setting Recruitment: Unclear Prospective or retrospective: (Unclear) probably prospective Sample size (cases): 240 (68) Additional inclusion criteria: Additional 189 matched samples used in the Phase 2 study; not extracted due to saliva samples having received additional treatment (omni bead mill homogeniser). Additional 5 samples used for pooling assessment; not extracted
Patient characteristics and setting	Setting: Mixed: OP (healthcare centre) and community setting Location: The Augusta University- CLIA laboratory Country: USA Dates: Not stated Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swabs Sample collection device: Sterile tube; no details Sample collected by: Healthcare worker Sample collection method: Sterile flocked swab Sample storage/transport: 3 mL of viral transport medium (Specimen Collection and Transport System BD Sterile). All samples were stored at 4 °C temperature and transported to the SARS-CoV-2 testing facility at Augusta University within 24 hours of sample collection. Timing of sample collection: NS NAT extraction method: NS

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Sahajpal 2021 (Continued)

Assay used: TaqMan-based real time PCR assay

Genetic target: N and ORF1ab genes

Threshold: Both or one of the targets ≤ 42

Blinding reported: NS

Threshold predefined: NS

Index Sample: Saliva spit

Sample collection device: sterile container (DNA/RNA Shield Saliva Sputum Collection Kit e DX, catalog number R1210-E; Zymo Research, Irvine, CA)

Sample collected by: Patient/parent-instructed but unclear if supervised

Sample collection method: Unclear (instructed but unclear if supervised)

Sample storage/transport: 2 mL of viral transport medium

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: the National Institute of Allergy and Infectious Diseases, a component of the National Institutes of Health, Department of Health and Human Services

Publication status: Published paper

Source: Journal of Molecular Diagnostics

Author COI: R.K. has received honoraria, travel funding, and research support from Illumina, Asuragen, Qiagen, and BMS. M.H. holds stock options at PerkinElmer Inc.

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

Sahajpal 2021 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	

Sahajpal 2021 (Continued)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point No

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Sahni 2021

Study characteristics

Patient Sampling	Design: Single group of symptomatic children attending an outpatient paediatric practice and scheduled for testing Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 567 (114) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Hospital outpatient Location: New Vaccine Surveillance Network- Houston site Country: United States of America Dates: April 10 to July 31, 2020 Symptoms and severity: Children reported fever and/or ≥ 1 ARI symptom (cough, ear-ache, nasal congestion, runny nose, sore throat, wheezing, shortness of breath/rapid or shallow breathing) with onset < 14 days prior to the outpatient visit Demographics: Age: Median (range): 5.0 (0, 1-18) Sex: 300/569 (52.7%) male

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Sahni 2021 (Continued)

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal

Sample collection device: Not stated

Sample collected by: Healthcare worker (HCW)

Sample collection method: Several commercial nylon and flocked swabs: Copan contoured nylon flocked swabs (Copan Diagnostics, Murrieta, California), iClean nylon flocked swabs (Huachenyang (Shenzhen) Technology Co., Ltd, Houston, Texas), Diagnostic Hybrids flocked swabs (Diagnostic Hybrids, Quidel Corporation, San Diego, California)

Sample storage/transport: Several viral transport media, no more details provided. Specimen types were placed in 3 mL of viral transport media and refrigerated for up to 5 hours.

Samples transported to research lab around 5 hours after collection

Timing of sample collection: median time between symptom onset and specimen collection was 4 days (range 1-14 days).

NAT extraction method: MagNA Pure 96 (Roche, Indianapolis, Indiana)

Assay used: RealStar® SARS-CoV-2 RT-PCR kit (Altona, Hamburg, Germany; n = 279 of 573 specimens) or Aptima® SARSCoV-2 Assay on the Hologic Panther® System (Hologic, Marlborough, Massachusetts; n = 294 of 573 specimens)

Genetic target: E and S genes or ORF1ab gene

Threshold: Ct value ≤ 45 or light reaction

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Nasal mid-turbinate

Sample collection device: Not stated

Sample collected by: Healthcare worker (HCW)

Sample collection method: Copan-contoured nylon flocked swabs with stopper and tapered

Nasal mid-turbinate samples collected before NPS

Sample storage/transport: BD universal viral transport media (Becton, Dickinson and Company, Franklin Lakes, New Jersey). Specimen types were placed in 3 mL of viral transport media and placed on ice for up to 5 hours. Samples transported to research lab around 5 hours after collection

Timing of sample collection: As for reference sample

NAT extraction method: QIAampViral mini RNA Kit (QIAGEN Sciences, Maryland)

Assay used: CDC EUA of CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time reverse transcriptase polymerase chain reaction (RT-PCR) Diagnostic Panel

Genetic target: N1 and N2 genes

Threshold: Ct value ≤ 40

Blinding reported: NS

Sahni 2021 (Continued)

Threshold predefined: Yes

Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes Missing data: 52 excluded for Rnase-P negative or no paired sample taken (Figure 1) Uninterpretable results: 2 samples inconclusive Indeterminate results: None reported
Comparative	
Notes	Funding: Texas Children's Hospital and the Centres for Disease Control and Prevention Publication status: Published paper Source: Journal of the Pediatric Infectious Disease Society Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

Sahni 2021 (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Yes

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Sahni 2021 (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

Salvatore 2021

Study characteristics

Patient Sampling	Design: Single group of index cases and their household members enrolled in a household transmission investigation in Utah (UT) and Wisconsin (WI) Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): 452 (121) Additional inclusion criteria: Insufficient information about relevant subgroup (PPA and NPA calculated using GEE); no extraction performed (only overall data) Raw data overall sample provided in suppl. material. Estimates of accuracy by subgroup (child versus adult; time pso; symptom status) only provided as summary estimates adjusted for repeated sampling
Patient characteristics and setting	Setting: Contact tracing Location: Utah and Wisconsin Country: USA Dates: March 22 to April 25, 2020 Symptoms and severity: 230/454 (51%) symptomatic Demographics: Age: Median (IQR): 27 (18-48); 55/226 (24%) < 18 yrs Sex: 109/226 (48%) males Exposure history: Not stated
Index tests	Reference sample: Nasopharyngeal swabs Sample collection device: Not stated Sample collected by: Healthcare worker Sample collection method: Nasopharyngeal specimens were collected by CDC clinicians from the patient's right nostril using BD flexible minitip flocked swabs. Sample storage/transport: Not stated Timing of sample collection: At the time of enrolment and 14 days later; in households where a member who tested negative at enrolment reported new symptoms during follow-up, additional specimens were collected from household members at the time of new symptom presentation. NAT extraction method: The QIAgen EZ1 Advanced XL or the bioMérieux EMAG Assay used: CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel

Salvatore 2021 (Continued)

Genetic target: N1 and N2 genes

Threshold: Results were considered positive if signal was detected (cycle threshold [Ct] < 40) for RP, N1, and N2 genes.

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Nasal mid-turbinate swab, single nostril

Sample collection device: Not stated

Sample collected by: Unsupervised patient (instructions provided)

Sample collection method: Samples were collected from left nostril (opposite to reference sample) using BD regular flocked swabs.

Sample storage/transport: Not stated

Timing of sample collection: Not stated

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: Specimen pairs in which at least one result was deemed inconclusive after re-testing or invalid (no signal from either N1, N2, or RP) were excluded (n = 15 specimens, 14 participants).

Comparative

Notes

Funding: Not stated

Publication status: Published Letter

Source: Journal of Clinical Virology

Author COI: Authors declared no COI present.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?

Unclear

Salvatore 2021 (Continued)

Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	No
Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	No
Could the selection of patients have introduced bias?	High risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	

Salvatore 2021 (Continued)

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point No

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Schwob 2020

Study characteristics

Patient Sampling	Design: Single group of adults with 'symptoms compatible with COVID-19 according to regional testing criteria' Recruitment: Unclear ('All patients having a result available for the 3 tests were included') Prospective or retrospective: Prospective Sample size (cases): 928 (385) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Lausanne Country: Switzerland Dates: September 25th to November 4th 2020 Symptoms and severity: Symptomatic: 891/928 (96%) at least one major symptom and 37/928 (4%) one minor symptom Demographics: Age: Median (IQR): 31 (25-42) Sex: 473/928 (51%) male Exposure history: Known exposure to COVID-19: 37/928 (4%)

Schwob 2020 (Continued)

Index tests

Reference sample: NPS

Sample collection device: NS

Sample collected by: HCW-collected. Laboratory-interpreted

Sample collection method: Collected after saliva. No further details

Sample storage/transport: NS

Timing of sample collection: Mean (SD): 2.6 (2.3) pso

NAT extraction method: NS

Assay used: In-house RT-PCR (automated molecular diagnostic platform), OR SARS-CoV-2 test of the Cobas 6800 instrument (Roche, Basel, Switzerland).

Genetic target: E gene

Threshold: 105 copies/mL (Ct = 30)

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva swab + drool

Sample collection device: NS

Sample collected by: Patient/parent-collected. Laboratory-interpreted

Sample collection method: Swabbing oral mucosa and finishing by drooling saliva in a tube. Collected prior to NPS

Sample storage/transport: NS

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: The saliva PCR was paid for by the Cantonal health authorities.

Schwob 2020 (Continued)

Publication status: Pre-print

Source: MedRxiv

Author COI: None stated

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Unclear		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			

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Schwob 2020 (Continued)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Low risk

Senok 2020

Study characteristics

Patient Sampling	Design: Single group of adult patients undergoing COVID-19 testing at the Al Khawaneej Health Centre in Dubai, United Arab Emirates (UAE). 'Contacts of confirmed positive cases, those with presumptive symptoms with or without history of contact with a confirmed case as well as individuals concerned about possible infection.' Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 401 (35) Additional inclusion criteria: None
Patient characteristics and setting	Setting: COVID-19 testing centre Location: Al Khawaneej Health Centre, Dubai Country: United Arab Emirates

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Senok 2020 (Continued)

Dates: 29 June to 14 July 2020

Symptoms and severity: 195/401 (48.6%) asymptomatic

Demographics: Age: Mean (SD): 35.5 (9.5)

Sex: 329/401 (82%) male

Exposure history: 176/401 (43.9%) with known exposure to COVID-19 case

Index tests

Reference sample: Nasopharyngeal

Sample collection device: Not stated

Sample collected by: Healthcare worker

Sample collection method: A COVID-19 screening protocol already in place at the facility was followed; no details provided

Sample storage/transport: Greiner Bio-One universal transport system (Greiner Bio-One, Kremsmünster, Austria). Paired swab and saliva samples were stored at room temperature within 3 hours of collection.

Timing of sample collection: Median (IQR) onset of symptoms prior to the test was 2.5 (1–14) days.

NAT extraction method: Chemagic viral RNA extraction kit on the automated Chemagic™ 360 Nucleic Acid Extractor (PerkinElmer, Baesweiler, Germany) according to the manufacturer's instructions

Assay used: NeoPlex COVID-19 kit (GeneMatrix, Seoul, South Korea)

Genetic target: RdRp and N genes

Threshold: If two gene targets or only the RdRp gene target was amplified. A cycle threshold of ≤ 40 was taken as cut-off for a positive result for both target genes.

Blinding reported: NS

Threshold predefined: NS

Index Sample: Saliva (drool)

Sample collection device: Sterile containers

Sample collected by: Unsupervised patient
'Healthcare personnel were trained in giving instructions to the patients for saliva collection and a unified script was used'.

Sample collection method: Patients were asked to pool saliva in their mouth for 1–2 minutes and then gently spit 2–4 mL of saliva into the provided sterile container at least one hour after the patient last consumed food, fluid, or smoked tobacco.

Sample storage/transport: Dry/direct sampling

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Senok 2020 (Continued)

Threshold predefined: As for reference sample

Target condition and reference standard(s)	
Flow and timing	Simultaneous sample collection: Yes
	Missing data: None reported
	Uninterpretable results: None reported
	Indeterminate results: None reported
Comparative	
Notes	Funding: No funding
	Publication status: Published paper
	Source: Infection and Drug resistance
	Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type in-	Unclear		

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Senok 2020 (Continued)

terpreted without knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias?

Unclear risk

Skolimowska 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP/OP and saliva samples Design: 132 (19) symptomatic HCWs and household contacts presenting to a dedicated COVID-19 outpatient clinic and with acute (< 7-day duration) symptoms meeting the Public Health England case definition. Recruitment: Appeared consecutive Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: dedicated COVID-19 outpatient clinic Location: Not stated; London hospital (author institutions included Imperial College Healthcare NHS Trust, and Chelsea and Westminster NHS Foundation Trust, London) Country: UK Dates: 28 April to 7 May 2020 Symptoms and severity: Described as 'mild community cases'. All symptomatic and < 7 days pso Demographics: Median age 39 y (IQR 30, 51 y); included 5 patients < 18 years. Sex: 43, 33% male Exposure history: Sample included household contacts and symptomatic HCW.
Index tests	Reference Sample: Naso/oropharangeal (NP/OP) Sample collected by: Trained HCW Sample collection method: Swab nos; both sides of the oropharynx, then nasopharynx swabbed Sample storage/transport: Collected in 4.3 mL of Roche Cobas® PCR medium; storage not described Timing of sample collection: All < 7 d pso NAT extraction method: Not stated Assay used: RT-PCR; one of an unspecified number of assays (from Roche, AusDiagnostics, ThermoFisher and Abbott), approved for detection of SARS-CoV-2 Genetic target: Not stated; PCR+ samples re-run using AusDiagnostics multiplex tandem RT-PCR, targeting ORF 1ab and 8 (annotated as target A and B, respectively) Threshold: Not stated Blinding reported: Not stated Threshold predefined: Assume yes Index Sample: saliva Sample collected by: Patient Sample collection method: Patient asked to spit into a sterile container, without preceding coughing Sample storage/transport: On receipt in the laboratory, 4.3 mL of Cobas® PCR medium was added to saliva; storage not described

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Skolimowska 2020 (Continued)

Timing of sample collection: All < 7d pso

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Assume yes

Target condition and reference stan-
dard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: same clinic visit

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: 1 saliva specimen was inhibited on testing.

Indeterminate results: None reported

Comparative

Notes

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
One author also acknowledged 'support from the (NIHR) Imperial Biomedical Research Centre (BRC) and the NIHR (HPRU) in Healthcare Associated Infection and Antimicrobial Resistance at Imperial College London in partnership with Public Health England'.

Publication status: Published

Source: Clinical Microbiology and Infection

Author COI: L.S.P.M. has consulted for bioMerieux (2013), DNA electronics (2015e2018), Dairy Crest (2017e2018), Umovis Lab (2020) and Pfizer (2018e2020), received speaker fees from Profile Pharma (2018), received research grants from the NIHR (2013e2020), CWp Charity (2018e2019) and Leo Pharma (2016), and received educational support from Eumedica (2016e2018). R.J. has received honoraria, speaker fees, travel support and/or research grant funding from Gilead, ViiV Healthcare and MSD. All other authors had no conflicts of interest to declare.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		

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Skolimowska 2020 (Continued)

Did the study avoid inappropriate inclusions?	Yes	
Was the intention that patients receive all tests at all time points?	Yes	
Could the selection of patients have introduced bias?		Unclear risk
Are there concerns that the included patients and setting do not match the review question?		Low concern
DOMAIN 2: Index test (Saliva)		
If a threshold was used, was it pre-specified?	Yes	
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear	
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes	
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear	
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear
DOMAIN 2: Index test (Gargle)		
DOMAIN 2: Index test (Oral swab)		
DOMAIN 2: Index test (Oropharyngeal)		
DOMAIN 2: Index test (Collection method)		
DOMAIN 2: Index test (Oropharyngeal/nasal)		
DOMAIN 2: Index test (Nasal)		
DOMAIN 2: Index test (Oral rinse)		
DOMAIN 2: Index test (Operator)		
DOMAIN 3: Reference standard		

Skolimowska 2020 (Continued)

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? High risk

Smith-Jeffcoat 2021
Study characteristics

Patient Sampling	Design: Single group of patients from several symptomatic and asymptomatic inpatient and outpatient departments of Grady Memorial Hospital, being tested due to diagnostic (e.g. patients were symptomatic or exposed) or screening (e.g. preoperative requirement or before admission for non-COVID-19 reasons) purposes Recruitment: Consecutive Prospective or retrospective: Prospective Sample size (cases): [A] ANS samples: 995 (78) [B] Saliva samples: 921 (73) Additional inclusion criteria: Missing data affected totals in numerical extraction.
Patient characteristics and setting	Setting: Mixed: Hospital IP and OP Location: Grady Memorial Hospital, Georgia, Atlanta Country: USA Dates: August 31 to November 23, 2020

Smith-Jeffcoat 2021 (Continued)

Symptoms and severity: 196/1006 (18.2%) sought care for a COVID-19 related concern. 329/1006 (30.6%) had a chief complaint including COVID-19 symptoms.

Demographics: Age: 614/1006 (57.1%) were > 50 years of age
Sex: 559/1006 (51.9%) male

Exposure history: Not stated

Index tests

Reference sample: Nasopharyngeal swab

Sample collection device: Not stated

Sample collected by: Healthcare worker (HCW)

Sample collection method: A nasopharyngeal swab (NPS) sample was collected by healthcare workers at Grady Memorial Hospital (Atlanta, Georgia, USA) using flocked foam swabs.

Sample storage/transport: 3 mL Smart Transport Medium (MedSchenker, <https://medschenker.com>). NPS samples were stored at 4 °C and remnant Smart Transport Medium was aliquoted and transferred to the US Centres for Disease Control and Prevention (CDC; Atlanta) laboratory for RT-PCR.

Timing of sample collection: Patients were tested for diagnostic (e.g. patients were symptomatic or exposed) or screening (e.g. preoperative requirement or before admission for non-COVID-19 reasons) purposes.

NAT extraction method: Maxwell RSC Viral Total Nucleic Acid Purification Kit (Promega)

Assay used: CDC 2019-nCoV Real-Time Reverse transcriptase PCR Diagnostic Panel

Genetic target: N1 and N2 targets

Threshold: Cycle threshold < 40 of both N1 and N2 gene targets were considered positive.

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Anterior nasal swab

Sample collection device: Not stated

Sample collected by: Unsupervised patient

Sample collection method: Patients were then advised to collect anterior nasal swab (ANS) samples by inserting a mini flocked tip swab into 1 anterior naris, twirling the swab for 10 s, removing the swab and placing it directly into the other naris, and twirling again for 10 s.

Sample storage/transport: 3 mL universal viral transport media (Becton, Dickinson and Company). All self-collected specimens were stored at 4 °C or frozen (ANS samples only) before extraction.

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Smith-Jeffcoat 2021 (Continued)

Threshold predefined: As for reference sample

Index Sample (B): Saliva nos

Sample collection device: A sterile 50 mL conical centrifuge tube

Sample collected by: Unsupervised patient

Sample collection method: Patients collected ≈2 mL raw saliva, after checking an infographic outlining steps for self-collection of saliva and ANS samples.

Sample storage/transport: Raw saliva; no more details provided

Timing of sample collection: All self-collected specimens were stored at 4 °C or frozen (ANS samples only) before extraction.

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: 69/1076 NP samples missing and not processed
82/1006 saliva samples not collected or not tested
8/1006 ANS samples not collected or not tested

Uninterpretable results: None reported

Indeterminate results:
1/1076 NP samples indeterminate and excluded for analysis
3/1006 saliva indeterminate and excluded for analysis
3/1006 ANS indeterminate and excluded for analysis

Comparative

Notes

Funding: CDC Foundation

Publication status: Published

Source: Emerging Infectious Diseases

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		

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Smith-Jeffcoat 2021 *(Continued)*

Did the study avoid inappropriate exclusions?	Yes
Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Low risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
If a threshold was used, was it pre-specified?	Yes

Smith-Jeffcoat 2021 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	No
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

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Teo 2021 (a)

Study characteristics

Patient Sampling	Design: Single group of migrant workers presenting with symptomatic ARI and asymptomatic roommates of newly diagnosed COVID-19 cases (n = 149) (a) Symptomatic participants tested using nasal anterior and saliva samples (n = 45) Prior confirmed cases not included in this review (n = 51). Results of repeated testing of individuals not included in this review. Results of repeated testing of saliva and nasal samples with an alternative RT-PCR test not included in this review Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 45 (29) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Community Location: Bed purpose-built dormitory and Singapore General Hospital (SGH), Singapore Country: Singapore Dates: Between 2nd and 26th June 2020 Symptoms and severity: 45/45 (100%) symptomatic Demographics: Not stated Exposure history: None with reported exposure to known COVID-19 case
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected/HCW-interpreted Sample collection method: NP swab collection procedure was performed by a trained researcher. Sample storage/transport: VTM. NP swabs were sent dry in cooler boxes to the Singapore General Hospital (SGH) molecular laboratory as part of routine clinical testing. All samples were processed on the same day. Timing of sample collection: NS NAT extraction method: Commercial kit by GeneAid Biotech Ltd. Assay used: Laboratory-developed RT-PCR test (CDC-LDT) on an automated Cobas 6800 system Genetic target: N1, N2 gene Threshold: Ct < 40 for positivity Blinding reported: NS Threshold predefined: Yes Index Sample (A): Saliva spit

Teo 2021 (a) (Continued)

Sample collection device: Container with 2 mL of viral RNA stabilisation fluid (SAFER-Sample Stabilisation Fluid, Lucence, Singapore)

Sample collected by: Supervised patient-collected/HCW-interpreted

Sample collection method: For the collection of naso-oro-pharyngeal saliva samples, participants were asked to tilt their head back slightly, clear their throat and nose, and spit the saliva into the collection bottle. The steps were repeated until the required volume (2 mL) was achieved. For “naso-oro-pharyngeal” saliva collection, instructional videos were shown.

Sample storage/transport: Viral RNA stabilisation fluid

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: Laboratory-developed RT-PCR test (CDC-LDT)
Fortitude 2.1 kit (MiRXES, Singapore)

Genetic target: N1, N2 gene, ORF1ab gene

Thresholds: Ct < 38 (https://www.hsa.gov.sg/docs/default-source/hprg-mdb/psar-covid-19-puo-tests/mo10_mirxes-fortitude-kit-2-1.pdf)

Blinding reported: NS

Threshold predefined: Yes

Index Sample (B): Single nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient-collected/HCW-interpreted

Sample collection method: Participants were instructed to insert the swab (about 1 cm) into their nostrils (one at a time), tilt their head back slightly, and rotate the swab in a circular motion for 3 times around the nasal wall. The swab was then inserted into the collection tube.

Sample storage/transport: VTM

Timing of sample collection: NS

NAT extraction method: Not stated

Assay used: Laboratory-developed RT-PCR test (CDC-LDT)
Fortitude 2.1 kit (MiRXES, Singapore)

Genetic target: N1, N2 gene, ORF1ab gene

Thresholds: Ct < 38 (https://www.hsa.gov.sg/docs/default-source/hprg-mdb/psar-covid-19-puo-tests/mo10_mirxes-fortitude-kit-2-1.pdf)

Blinding reported: NS

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Teo 2021 (a) (Continued)

Indeterminate results: None reported

Comparative

Notes

Funding: This work was supported by a grant from the Changi Airport Group. Fortitude 2.1 kits were provided by the Diagnostics Development Hub (DxD Hub), Accelerate, Agency for Science, Technology and Research, Singapore. The study sponsor had no role in the design, implementation, analysis or write-up of the study.

Publication status: Published paper

Source: Nature Scientific Reports

Author COI: Yukti Choudhury, Chae Yin Cher, Zi Yi Wan, and Min Han Tan are employees of, and affiliated with, Lucence. Y.C. and M.H.T. are shareholders of Lucence; M.H.T. is a director of Lucence. An affiliated entity of Lucence is the applicant of certain patent applications for relevant diagnostics. Y.C., C.Y.C. and/or M.H.T. are named inventors for some of these patent applications. At the time of this research, patents were pending for the next-generation sequencing approach and the saliva testing process discussed in the manuscript.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type	Yes		

Teo 2021 (a) *(Continued)*

unlikely to advantage one of the sample types?

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?

Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Gargle)

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified?

Yes

Is undergoing one sample type unlikely to influence the result of the other sample type?

Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?

Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?

Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Teo 2021 (a) *(Continued)*

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Unclear risk

Teo 2021 (b)
Study characteristics

Patient Sampling	Design: Single group of migrant workers presenting with symptomatic ARI and asymptomatic roommates of newly diagnosed COVID-19 cases (n = 149) (b) Asymptomatic participants using nasal and saliva samples (n = 104) Prior confirmed cases not included in this review (n = 51). Results of repeated testing of individuals not included in this review. Results of repeated testing of saliva and nasal samples with an alternative RT-PCR test not included in this review Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 104 (37) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Community Location: Bed purpose-built dormitory and Singapore General Hospital (SGH), Singapore Country: Singapore

Teo 2021 (b) (Continued)

Dates: Between 2nd and 26th June 2020

Symptoms and severity: 0/104 (0%) symptomatic

Demographics: Not stated

Exposure history: 104/104 (100%) with known exposure to COVID-19 case (close contacts)

Index tests

Reference sample: NP swab

Sample collection device: Not stated

Sample collected by: HCW-collected/HCW-interpreted

Sample collection method: NP swab collection procedure was performed by a trained researcher.

Sample storage/transport: VTM

Timing of sample collection: NP swabs were sent dry in cooler boxes to the Singapore General Hospital (SGH) molecular laboratory as part of routine clinical testing. All samples were processed on the same day.

NAT extraction method: Commercial kit by GeneAid Biotech Ltd

Assay used: Laboratory-developed RT-PCR test (CDC-LDT) on an automated Cobas 6800 system

Genetic target: N1, N2 gene

Threshold: Ct < 40 for positivity

Blinding reported: NS

Threshold predefined: Yes

Index Sample (A): Saliva spit

Sample collection device: Container with 2 mL of viral RNA stabilisation fluid (SAFER-Sample Stabilisation Fluid, Lucence, Singapore)

Sample collected by: Supervised patient-collected/HCW-interpreted

Sample collection method: For the collection of naso-oro-pharyngeal saliva samples, participants were asked to tilt their head back slightly, clear their throat and nose, and spit the saliva into the collection bottle. The steps were repeated until the required volume (2 mL) was achieved. For "naso-oro-pharyngeal" saliva collection, instructional videos were shown.

Sample storage/transport: Viral RNA stabilisation fluid

Timing of sample collection: NS

NAT extraction method: As for reference sample

Assay used: Laboratory-developed RT-PCR test (CDC-LDT)
Fortitude 2.1 kit (MiRXES, Singapore)

Genetic target: N1, N2 gene, ORF1ab gene

Thresholds: Ct < 38 (https://www.hsa.gov.sg/docs/default-source/hprg-mdb/psar-covid-19-puo-tests/mo10_mirxes-fortitude-kit-2-1.pdf)

Blinding reported: NS

Teo 2021 (b) (Continued)

Threshold predefined: Yes

Index Sample (B): Single nasal anterior nares swab

Sample collection device: Not stated

Sample collected by: Supervised patient-collected/HCW-interpreted

Sample collection method: Participants were instructed to insert the swab (about 1 cm) into their nostrils (one at a time), tilt their head back slightly, and rotate the swab in a circular motion for 3 times around the nasal wall. The swab was then inserted into the collection tube.

Sample storage/transport: VTM

Timing of sample collection: NS

NAT extraction method: Not stated

Assay used: Laboratory-developed RT-PCR test (CDC-LDT)
Fortitude 2.1 kit (MiRXES, Singapore)

Genetic target: N1, N2 gene, ORF1ab gene

Thresholds: Ct < 38 (https://www.hsa.gov.sg/docs/default-source/hprg-mdb/psar-covid-19-puo-tests/mo10_mirxes-fortitude-kit-2-1.pdf)

Blinding reported: NS

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: This work was supported by a grant from the Changi Airport Group. Fortitude 2.1 kits were provided by the Diagnostics Development Hub (DxD Hub), Accelerate, Agency for Science, Technology and Research, Singapore. The study sponsor had no role in the design, implementation, analysis or write-up of the study.

Publication status: Published paper

Source: Nature Scientific Reports

Author COI: Yukti Choudhury, Chae Yin Cher, Zi Yi Wan, and Min Han Tan are employees of, and affiliated with, Lucence. Y.C. and M.H.T. are shareholders of Lucence; M.H.T. is a director of Lucence. An affiliated entity of Lucence is the applicant of certain patent applications for relevant diagnostics. Y.C., C.Y.C. and/or M.H.T. are named inventors for some of these patent applications. At the time of this research, patents were pending for the next-generation sequencing approach and the saliva testing process discussed in the manuscript.

Methodological quality

Teo 2021 (b) (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			

Teo 2021 (b) (Continued)

DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point? Yes

Teo 2021 (b) *(Continued)*

Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

Torres 2021
Study characteristics

Patient Sampling	Design: Paired NP and saliva spit samples from self-reported mild symptomatic or asymptomatic individuals Recruitment: Unclear Prospective or retrospective: Prospective Sample size (cases): 972 (104) Additional inclusion criteria: Discrepancy between some reported results in text and table 1. I have used table 1 for extraction as these are more internally consistent.
Patient characteristics and setting	Setting: COVID-19 testing centre 'Community testing sites' Location: Tucson Country: Arizona Dates: Late July to early September 2020 Symptoms and severity: 54/107 (51%) test positives were symptomatic. Demographics: Age: Mean 34.7 (site 1); 47.8 (site 2) Sex: Not stated Exposure history: Not stated
Index tests	Reference sample: NP swab Sample collection device: Not stated Sample collected by: HCW-collected. Laboratory-collected Sample collection method: Self-collection of saliva followed by NPS collection Sample storage/transport: All samples were processed within 12 h of collection. No further details Timing of sample collection: 23/972 (2%) had symptoms > 14 days. NAT extraction method: RNAdvance Viral XP Reagent kit extraction (Beckman) Assay used: CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel with One Step Primer Script III RT-PCR Kit (Takara Bio Inc. Japan)

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Torres 2021 (Continued)

Blinding reported: N gene (<https://www.fda.gov/media/134922/download>)

Genetic target: N gene

Threshold: Ct < 40 (<https://www.fda.gov/media/134922/download>) CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel with One Step Primer Script III RT-PCR Kit (Takara Bio Inc. Japan)

Blinding reported: NS (<https://www.fda.gov/media/134922/download>)

Threshold predefined: Yes

Index Sample: Saliva spit

Sample collection device: SDNA-1000 Saliva Collection device (Spectrum Solutions LLC, USA) OR sterile dry 50 mL conical vial

Sample collected by: Unsupervised patient-collected. Laboratory-interpreted

Sample collection method: Self-collection of saliva was performed using either the SDNA-1000 Saliva Collection device (Spectrum Solutions LLC, USA) or a sterile dry 50 mL conical vial

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Not stated

Uninterpretable results: Not stated

Indeterminate results: Not stated

Comparative

Notes

Funding: This research did not receive any specific grant from funding agencies.

Publication status: Published paper

Source: Academic journal (Journal of Infection)

Author COI: No COI statement reported

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

Torres 2021 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	

Torres 2021 *(Continued)*
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Tu 2020 [A]
Study characteristics

Patient Sampling	Single-group study to evaluate agreement between NP, nasal mid-turbinate, nasal anterior and oral (tongue) samples Design: 530 patients presenting with symptoms indicative of upper respiratory infection (subjective and objective fevers, cough, sore throat, fevers, myalgia, or rhinorrhoea) at one of five ambulatory clinics. Per pairwise comparison: NP-tongue 501 (49) NP-nasal 498 (50) NP-MT 504 (52) Recruitment: Unclear Prospective or retrospective: Unclear (appears to be prospective) Exclusion criteria: Those who were not able to demonstrate understanding of the study, unwilling to commit to all four samples, with a history of nosebleeds in the past 24 hours, nasal surgery in the past two weeks, chemotherapy treatment with documented low platelet and low white blood cell counts, or acute facial trauma
Patient characteristics and setting	Setting: Outpatient/community settings (ambulatory care) Location: Five ambulatory clinics in the Puget Sound Region of Washington; no further details Country: USA

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Tu 2020 [A] (Continued)

Dates: March 16 to March 21, 2020

Symptoms and severity: Reported separately for patients in each pairwise comparison; extracted here for the largest reported sample (nasal MT & NP samples, n = 504): fever 74, 15%; ear pain/drainage 135, 28%; vomiting 46, 9%; cough 388, 77%; diarrhoea 150, 30%; difficulty breathing 253, 50%

Demographics: Age range: 15 months to 94 years old;
Age < 30 116, 23%; 30-39 116, 23%; 40-49 92, 18%; 50-59 87, 17%; ≥ 60 93, 18%
Sex: 201, 40% male

Exposure history: Not reported

Index tests

Reference Sample: Nasopharyngeal (NP)

Sample collected by: HCW

Sample collection method: 1) pass the swab (polyester-tipped swab on a skinny wire (Puritan 25-800-2PDBG) along the floor of the nose until meeting gentle resistance as the swab touches the posterior pharynx, in the nostril corresponding to the patient's dominant hand, and 2) rotate the swab several times and withdraw.

Sample collection method:

Sample storage/transport: Stored in VTM at 4 °C before shipping (volume not reported)

Timing of sample collection: On presentation; time pso reported per pairwise comparison mean (SD):

NP-tongue +ve cases 6.8 days (SD 5.3); -ve cases 7.1 days (SD 8.0)

NP-nasal +ve cases 6.7 days (SD 5.4); -ve cases 7.1 days (SD 7.9)

NP-MT +ve cases 6.7 days (SD 5.2); -ve cases 6.9 days (SD 7.7)

NAT extraction method: Not stated

Assay used: rRT-PCR (Quest Diagnostics, San Juan Capistrano, CA)

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated; presume yes

Index Sample [C] Nasal anterior

Sample collected by: patient

Sample collection method: Nasal samples were collected with a foam swab (Puritan 25-1506 1PF100) via the following steps: 1) gently inserting the swab in the vertical position into one nasal passage until there is gentle resistance, 2) leaving the swab in place for 10-15 seconds, rotating the swab, and 3) repeating the procedure on the other side with the same swab

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Tu 2020 [A] (Continued)

Threshold predefined: Assume yes

Index Sample [B]: Nasal mid-turbinate

Sample collected by: Patient

Sample collection method: 1) inserting the swab (nylon flocked swab (MDL NasoSwab A362CS02.MDL, 56380CS01 for adults and 56780CS01 for paediatrics)) in the horizontal position until gentle resistance was met, 2) leaving the swab in for 10 to 15 seconds on each side, rotating the swab, 3) repeating in the other nostril with the same swab

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Assume yes

Index sample [A]: Oral (tongue)

Sample collected by: Patient

Sample collection method: 1) Extending the tongue, and 2) firmly but gently brushing the swab (Nylon flocked swab (Copan FLOQSwab 502CS01)) along the length of the anterior 2/3 of dorsum of the tongue for 10 seconds

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Assume yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes: Patient samples obtained first (tongue, nasal anterior, then nasal mid-turbinate); then HCP took NP swabs.

Time interval between sampling methods: Simultaneously

All patients received all sampling methods: No, not all patients collected all samples.

Missing data: Total of 530 patients reported; so missing data per pairwise comparison: NP-tongue 29, NP-nasal 32, NP-MT 26

Uninterpretable results: None reported

Tu 2020 [A] (Continued)

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement reported

Publication status: Published

Source: NEJM

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
If a threshold was used, was it pre-specified?	Unclear		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes		
Were differences in the conduct or interpretation of tests for each sample type unlikely	Yes		

Tu 2020 [A] *(Continued)*

to advantage one of the sample types?

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?

Unclear

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Unclear

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?

Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point

No

Were the proportions and reasons for missing data similar

No

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Tu 2020 [A] (Continued)
across sample types (index
test)?

Were results presented per pa- Yes
tient?

Were all patients included in No
the analysis?

**Could the patient flow have High risk
introduced bias?**

Tu 2020 [B]

Study characteristics

Patient Sampling	Single-group study to evaluate agreement between NP, nasal mid-turbinate, nasal anterior and oral (tongue) samples Design: 530 patients presenting with symptoms indicative of upper respiratory infection (subjective and objective fevers, cough, sore throat, fevers, myalgia, or rhinorrhoea) at one of five ambulatory clinics. Per pairwise comparison: NP-tongue 501 (49) NP-nasal 498 (50) NP-MT 504 (52) Recruitment: unclear Prospective or retrospective: unclear (appears to be prospective) Exclusion criteria: Those who were not able to demonstrate understanding of the study, unwilling to commit to all four samples, with a history of nosebleeds in the past 24 hours, nasal surgery in the past two weeks, chemotherapy treatment with documented low platelet and low white blood cell counts, or acute facial trauma
Patient characteristics and setting	Patient/community settings (ambulatory care) Location: five ambulatory clinics in the Puget Sound Region of Washington; no further details Country: USA Dates: March 16 to March 21, 2020 Symptoms and severity: reported separately for patients in each pairwise comparison; extracted here for the largest reported sample (nasal MT & NP samples, n = 504): fever 74, 15%; ear pain/drainage 135, 28%; vomiting 46, 9%; cough 388, 77%; diarrhoea 150, 30%; difficulty breathing 253, 50% Demographics: Age range: 15 months to 94 years old; Age < 30 116, 23%; 30-39 116, 23%; 40-49 92, 18%; 50-59 87, 17%; ≥ 60 93, 18% Sex: 201, 40% male Exposure history: Not reported
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: HCW

Tu 2020 [B] (Continued)

Sample collection method: 1) pass the swab (polyester-tipped swab on a skinny wire (Puritan 25-800-2PDBG) along the floor of the nose until meeting gentle resistance as the swab touches the posterior pharynx, in the nostril corresponding to the patient's dominant hand, and 2) rotate the swab several times and withdraw.

Sample collection method:

Sample storage/transport: Stored in VTM at 4 °C before shipping (volume not reported)

Timing of sample collection: On presentation; time pso reported per pairwise comparison mean (SD):

NP-tongue +ve cases 6.8 days (SD 5.3); -ve cases 7.1 days (SD 8.0)

NP-nasal +ve cases 6.7 days (SD 5.4); -ve cases 7.1 days (SD 7.9)

NP-MT +ve cases 6.7 days (SD 5.2); -ve cases 6.9 days (SD 7.7)

NAT extraction method: Not stated

Assay used: rRT-PCR (Quest Diagnostics, San Juan Capistrano, CA)

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated; presume yes

Index Sample [B]: Nasal (mid-turbinate)

Sample collected by: Patient

Sample collection method: 1) gently inserting the swab (foam swab (Puritan 25-1506 1PF100) in the vertical position into one nasal passage until there is gentle resistance, 2) leaving the swab in place for 10-15 seconds, rotating the swab, and 3) repeating the procedure on the other side with the same swab

Sample storage/transport: As for reference sample

Timing of sample collection: As for rference sample

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Assume yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes: Patient samples obtained first (tongue, nasal anterior then nasal mid-turbinate); then HCP took NP swabs.

Time interval between sampling methods: Simultaneously

All patients received all sampling methods: No, not all patients collected all samples.

Missing data: Total of 530 patients reported; so missing data per pairwise comparison:

NP-tongue 29, NP-nasal 32, NP-MT 26

Uninterpretable results: None reported

Tu 2020 [B] (Continued)

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement reported

Publication status: Published

Source: NEJM

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			
If a threshold was used, was it pre-specified?	Yes		

Tu 2020 [B] *(Continued)*

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	No
Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	No
Were all patients included in the analysis?	Yes

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Tu 2020 [B] (Continued)

Could the patient flow have introduced bias?

High risk

Tu 2020 [C]
Study characteristics

Patient Sampling	Single-group study to evaluate agreement between NP, nasal mid-turbinate, nasal anterior and oral (tongue) samples Design: 530 patients presenting with symptoms indicative of upper respiratory infection (subjective and objective fevers, cough, sore throat, fevers, myalgia, or rhinorrhoea) at one of five ambulatory clinics. Per pairwise comparison: NP-tongue 501 (49) NP-nasal 498 (50) NP-MT 504 (52) Recruitment: Unclear Prospective or retrospective: Unclear (appears to be prospective) Exclusion criteria: Those who were not able to demonstrate understanding of the study, unwilling to commit to all four samples, with a history of nosebleeds in the past 24 hours, nasal surgery in the past two weeks, chemotherapy treatment with documented low platelet and low white blood cell counts, or acute facial trauma
Patient characteristics and setting	Setting: Outpatient/community settings (ambulatory care) Location: Five ambulatory clinics in the Puget Sound Region of Washington; no further details Country: USA Dates: March 16 to March 21, 2020 Symptoms and severity: Reported separately for patients in each pairwise comparison; extracted here for the largest reported sample (nasal MT & NP samples, n = 504): fever 74, 15%; ear pain/drainage 135, 28%; vomiting 46, 9%; cough 388, 77%; diarrhoea 150, 30%; difficulty breathing 253, 50% Demographics: Age range: 15 months to 94 years old; Age < 30 116, 23%; 30-39 116, 23%; 40-49 92, 18%; 50-59 87, 17%; ≥ 60 93, 18% Sex: 201, 40% male Exposure history: Not reported
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: HCW Sample collection method: 1) pass the swab (polyester-tipped swab on a skinny wire (Puritan 25-800-2PDBG) along the floor of the nose until meeting gentle resistance as the swab touches the posterior pharynx, in the nostril corresponding to the patient's dominant hand, and 2) rotate the swab several times and withdraw. Sample collection method: Sample storage/transport: Stored in VTM at 4 °C before shipping (volume not reported) Timing of sample collection: On presentation; time pso reported per pairwise comparison mean (SD):

Tu 2020 [C] (Continued)

NP-tongue +ve cases 6.8 days (SD 5.3); -ve cases 7.1 days (SD 8.0)
NP-nasal +ve cases 6.7 days (SD 5.4); -ve cases 7.1 days (SD 7.9)
NP-MT +ve cases 6.7 days (SD 5.2); -ve cases 6.9 days (SD 7.7)

NAT extraction method: Not stated

Assay used: rRT-PCR (Quest Diagnostics, San Juan Capistrano, CA)

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated; presume yes

Index Sample [B]: Nasal (mid-turbinate)

Sample collected by: Patient

Sample collection method: 1) inserting the swab (nylon flocked swab (MDL NasoSwab A362CS02.MDL, 56380CS01 for adults and 56780CS01 for paediatrics)) in the horizontal position until gentle resistance was met, 2) leaving the swab in for 10 to 15 seconds on each side, rotating the swab, 3) repeating in the other nostril with the same swab

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Not stated

Index Sample [C]: Nasal (anterior)

Sample collected by: Patient

Sample collection method: 1) gently inserting the swab (foam swab (Puritan 25-1506 1PF100)) in the vertical position into one nasal passage until there is gentle resistance, 2) leaving the swab in place for 10-15 seconds, rotating the swab, and 3) repeating the procedure on the other side with the same swab

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Assume yes

Target condition and reference
standard(s)

Tu 2020 [C] (Continued)

Flow and timing	Sampling schedule prespecified: Yes: Patient samples obtained first (tongue, nasal anterior then nasal mid-turbinate); then HCP took NP swabs.		
	Time interval between sampling methods: Simultaneously		
	All patients received all sampling methods: No, not all patients collected all samples.		
	Missing data: Total of 530 patients reported; so missing data per pairwise comparison: NP-tongue 29, NP-nasal 32, NP-MT 26		
	Uninterpretable results: None reported		
	Indeterminate results: None reported		
Comparative			
Notes	Funding: No funding statement reported		
	Publication status: Published		
	Source: NEJM		
	Author COI: No COI statement reported		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			

Tu 2020 [C] (Continued)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, dif-

Tu 2020 [C] (Continued)

ferent collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? No

Could the patient flow have introduced bias? High risk

Uddin 2021

Study characteristics

Patient Sampling Design: Single group of suspected patients (aged > 10 years) and contacts of confirmed COVID-19 cases with or without the signs and symptoms of COVID-19, attending a COVID-19 screening unit

Recruitment: Unclear

Prospective or retrospective: Prospective

Sample size (cases): 596 (231)

Additional inclusion criteria: Insufficient information to build the 2 x 2 table by days of symptoms and asymptomatic/symptomatic status

Patient characteristics and setting Setting: COVID-19 testing centre/drive-through
Location: Dhaka Hospital
Country: Bangladesh
Dates: July to November 2020
Symptoms and severity: 546/596 (92%) symptomatic
Demographics: Age (median- IQR): 32, 26-42
Sex: 338/596 (56.7%) male
Exposure history: Not stated

Index tests **Reference sample:** Nasopharyngeal swab
Sample collection device: Not stated
Sample collected by: HCW
Sample collection method: The NPS was collected in the VTM by a trained nurse according to the standard procedure described previously.
Sample storage/transport: VTM. Paired saliva and NPS were stored in a cool box until transported to the laboratory.

Uddin 2021 (Continued)

Timing of sample collection: NS

NAT extraction method: QIAamp viral RNA mini kit (Qiagen, Germany)

Assay used: iTaq universal probes one-step RT-qPCR kit

Genetic target: RdRp and N genes

Threshold: CT values of one or both target genes were ≤ 37

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Saliva salivate

Sample collection device: Sterile container, no details provider

Sample collected by: Supervised patient

Sample collection method: Healthcare workers instructed the participants to avoid taking food, drinking water, brushing teeth, washing mouth, coughing, and sniffing before saliva collection. A flocked swab was kept under the tongue for 2 to 3 min to pool the saliva in the mouth and gently spit 1 to 2 mL of saliva into a sterile container without the transport medium.

Sample storage/transport: Dry/direct. Paired saliva and NPS were stored in a cool box until transported to the laboratory.

Timing of sample collection: As for reference sample

NAT extraction method: Not stated

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: United States Agency for International Development (USAID)

Publication status: Published paper

Source: Microbiology Spectrum

Author COI: No COI statement reported

Methodological quality

Uddin 2021 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
DOMAIN 2: Index test (Nasal)			

Uddin 2021 (Continued)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Unclear

Were results presented per patient? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Unclear risk

Vaz 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP/OP and saliva samples for the diagnosis of COVID-19 Design: 155 (73) healthcare workers presenting with signs/symptoms suggestive of SARS-CoV-2 infection, and patients at the COVID-19 ward (later described as not hospitalised; number per group not stated) Recruitment: Not stated Prospective or retrospective: Not stated
Patient characteristics and setting	Setting: Unclear; described as 'inside the hospital area' Location: Complexo Hospitalar, Professor Edgard Santos (C-HUPES), Federal University of Bahia, Salvador Country: Brazil Dates: Not stated

Vaz 2020 (Continued)

Symptoms and severity: All symptomatic (described as mild-to-moderate for COVID-19 cases); no hospitalisations, intubation or deaths. Most common symptoms: headache (61.2%), cough (45.1%), myalgia (40.3%), sore throat (37.3%), fever (27.6%), anosmia (21.6%), aguesia (20.9%)

Demographics: median age 40 y (IQR 33 y, 48.5 y); 46 (31%) male

Exposure history: Not stated

Index tests

Reference Sample: Naso/oropharyngeal (NP/OP)

Sample collected by: Not stated

Sample collection method: Swab nos

Sample storage/transport: Nasopharyngeal and oropharyngeal specimens were sent to Bahia Central Laboratory (LACEN), a State Reference Laboratory; no further details

Timing of sample collection: median 4 days pso (IQR 3, 6)

NAAT extraction method: Not stated

Assay used: RT-PCR (BIOMOL OneStep/ COVID-19 Kit; Paraná Molecular Biology Institute)

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Yes

Threshold predefined: Assume yes

Index Sample: Saliva

Sample collected by: Patient

Sample collection method: instructed to repeatedly spit until approximately 2 mL of sample was obtained, thus avoiding mucous secretions from the oropharynx or lower respiratory tract (i.e. sputum).
Collected in a sterile urine cup

Sample storage/transport: Transported to LAPI in a thermal box at 2 to 8 °C, and stored at -80 °C until nucleic acid extraction (within 6 h of collection where possible)

Timing of sample collection: median 4 days pso (IQR 3, 6)

NAAT extraction method: QIAGEN QIAamp® RNA Mini Kit (diluted with PBS prior to extraction)

Assay used: RT-PCR; Charité-Berlin protocol

Genetic target: E gene, RdRp

Threshold: ≤ 40 Ct; both E and RdRp targets detected

Blinding reported: Yes

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Vaz 2020 (Continued)

Time interval between sampling methods: Same clinic session

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement reported

Publication status: Published

Source: Brazilian Journal of Infectious Diseases

Author COI: author declared no conflicts of interest.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	No		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Yes		

Vaz 2020 (Continued)

Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Vermeiren 2020
Study characteristics
The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Vermeiren 2020 (Continued)

Patient Sampling	Single-group study to estimate agreement between NP and nasal mid-turbinate samples for the diagnosis of COVID-19 Design: Single group study including: - COVID-19 symptomatic inpatients, outpatients, and emergency department patients across five hospitals (n = 94) Recruitment: Not stated Prospective or retrospective: Not stated, probably prospective Sample size (cases): 94 (35 BD Max, or 34 Rotor Gene) Additional inclusion criteria: No further details
Patient characteristics and setting	Setting: Mixed (inpatients, outpatients, ED) Location: Five hospitals; author institutions include: Shared Hospital Laboratory, Toronto; Department of Laboratory Medicine and Pathobiology, University of Toronto; Sunnybrook Health Sciences Centre; Department of Pathology and Molecular Medicine, McMaster University; Research Institute of St. Joe's Hamilton; all Ontario Country: Canada Dates: Not stated Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: Not stated Sample collection method: FLOQSwab nasopharyngeal swab (Copan UTM system; Copan, Italy; catalog no. 305C); no further details Sample storage/transport: universal transport medium (Copan UTM system) Timing of sample collection: Not stated NAT extraction method: ExK TNA-2 extraction strip Assay used: BD Max System (Becton, Dickinson, USA) Genetic target: SARS-CoV-2 UTR'5 region Threshold: Not stated Blinding reported: Not stated Threshold predefined: Assume yes Index Sample: Nasal mid-turbinate Sample collected by: Not stated Sample collection method: 'mid-turbinate sampling' using flocked regular nylon tip swab (ESwab collection system; catalog no. 480C); no further details Sample storage/transport: liquid Amies Timing of sample collection: Not stated

Vermeiren 2020 (Continued)

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: SARS-CoV-2 UTR'5 region

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Assume yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Not stated

Time interval between sampling methods: Simultaneous

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: (2) Rotor-gene, 1 pair of swabs could not be analysed (disqualified)

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement reported

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled?	Unclear		

Was a case-control design avoided?	Yes		

Did the study avoid inappropriate exclusions?	Unclear		

Did the study avoid inappropriate inclusions?	Unclear		

Was the intention that patients receive all tests at all time points?	Yes		

Could the selection of patients have introduced bias?		Unclear risk	

Are there concerns that the included patients and setting do not match the review question?			Unclear

Vermeiren 2020 (Continued)

DOMAIN 2: Index test (Saliva)
DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)
DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)

If a threshold was used, was it pre-specified? Unclear

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests? Yes

Vermeiren 2020 (Continued)

(samples, different collection methods) at each time point

Were the proportions and reasons for missing data similar across sample types (index test)?	No
Were results presented per patient?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	High risk

Villar 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and saliva samples for the diagnosis of COVID-19 Design: 13 (9) volunteers with and without liver disease (hepatitis) (n = 13; 5 with hepatitis) Recruitment: Convenience Prospective or retrospective: Retrospective
Patient characteristics and setting	Setting: Unclear Location: Not stated; author institution is Oswaldo Cruz Institute, FIOCRUZ, Rio de Janeiro Country: Brazil Dates: Not stated Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal NP Sample collected by: Not stated Sample collection method: Swab nos Sample storage/transport: Not stated Timing of sample collection: Not stated; some > 7 days pso NAAT extraction method: QIAamp Viral RNA Mini Kit, QIAGEN, Germany Assay used: RT-PCR; 2019-nCoV CDC EUA Kit, Integrated DNA Technologies, Coralville, USA Genetic target: Not stated Threshold: Not stated

Villar 2020 (Continued)

Blinding reported: Not stated

Threshold predefined: Yes; commercial kit

Index Sample: Saliva

Sample collection device: Salivette Device; manufacturer not stated

Sample collected by: Self-collected

Sample collection method: Salivette Device

Sample storage/transport: Not stated

Timing of sample collection: Not stated; some > 7 days pso

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Not stated

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement reported

Publication status: Published letter

Source: Journal of Infection

Author COI: No COI statement reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Unclear		

Villar 2020 (Continued)

Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	High risk
Are there concerns that the included patients and setting do not match the review question?	Unclear
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	

Villar 2020 (Continued)

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests?	Unclear
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear
Were results presented per patient?	Unclear
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Vlek 2020
Study characteristics

Patient Sampling	Single-group study to estimate agreement between different NP and OP/nasal mid-turbinate samples for the diagnosis of COVID-19 Design: 107 (27) healthcare workers with symptoms of COVID-19 such as cough, fever, sore throat, dyspnoea, or loss of smell and taste, and within 24 to 48 h of symptom onset Recruitment: Not stated Prospective or retrospective: Prospective
Patient characteristics and setting	Setting: Unclear; probably 'outpatient'/ambulatory Location: Diaconessenhuis Utrecht (general hospital), Utrecht Country: the Netherlands Dates: 21 to 29 April 2020 Symptoms and severity: All subjects showed symptoms of COVID-19 such as cough, fever, sore throat, dyspnoea, or loss of smell and taste. Demographics: Median age 34 y (range 19 to 63 y) Sex: not stated Exposure history: All HCW
Index tests	Reference Sample: Nasopharyngeal NP Sample collected by: team of nurses Sample collection method: ultra-thin applicator swab with flocked nylon fibre tip; swabbed one nostril until reaching the back of the nasopharyngeal cavity

Vlek 2020 (Continued)

and rotated before removal (Eswab Collection system, Copan, Italy, catalog No. 483C)

Sample storage/transport: 1 mL liquid Amies medium; transported to the microbiology laboratory where PCR testing was performed on the same day

Timing of sample collection: > 24 h but ≤ 48h pso

NAAT extraction method: Magnapure MP24 total NA kit (Roche, Almere, the Netherlands)

Assay used: RT-PCR; in-house according to Corman and colleagues (Charite-Berlin protocol)

Genetic target: Not stated

Threshold: < 40 Ct

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Oropharyngeal/nasal mid-turbinate (OP/nasal)

Sample collected by: team of nurses

Sample collection method: regular swabs with flocked nylon fibre tip; rear wall of the oropharynx and the lower nasal cavity using the same swab (Eswab Collection system, Copan, Italy, catalog No. 490CE)

Sample storage/transport: 1 mL liquid Amies medium; transported to the microbiology laboratory where PCR testing was performed on the same day

Timing of sample collection: > 24 h but ≤ 48h pso

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: Not stated

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes

Time interval between sampling methods: Same clinic session

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement reported

Publication status: Published

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Vlek 2020 (Continued)

Source: European Journal of Microbiology and Infectious Diseases

Author COI: Authors declared that they had no conflict of interest.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
DOMAIN 2: Index test (Oral swab)			
DOMAIN 2: Index test (Oropharyngeal)			
DOMAIN 2: Index test (Collection method)			
DOMAIN 2: Index test (Oropharyngeal/nasal)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Vlek 2020 (Continued)

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
DOMAIN 2: Index test (Operator)
DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Walker 2021
Study characteristics

Patient Sampling

Design: Single group of healthcare workers in a variety of roles in inpatient settings who enrolled in the SAFER Study, serially sampled with OP/nasal and saliva samples during the 12-week study period
A subgroup of 225 paired (on the same day) samples used for test accuracy estimation in this review. Note 85 individuals contributed multiple samples.

Recruitment: Unclear

Prospective or retrospective: Retrospective

Sample size (cases): 225 (20)

Additional inclusion criteria: Info available for COVID-19+ during the study period (85 participants, no paired samples; not extracted here)

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Walker 2021 (Continued)

1425 OP/nasal samples and 530 saliva samples collected over the 12-week study period. Only 225 paired (same day) samples used in this review.

Patient characteristics and setting

Setting: Other (HCW) in inpatient settings

Location: Royal Liverpool University Hospital (RLUH), University Hospitals NHS Foundation Trust

Country: UK

Dates: March 30 to April 9, 2020

Symptoms and severity: 40/85 (47.1) experienced any symptoms

Demographics: Age: Median (IQR): 35 (27.5-46.5)

Sex: 19/85 (22.4) males

Exposure history: Not stated, but some exposed to COVID-19 cases

Index tests

Reference sample: Nasopharyngeal /oropharyngeal swab

Sample collection device: Not stated

Sample collected by: Unsupervised patient (HCW)

Sample collection method: Participants were asked to provide a self-collected OP/ nasal sample by swabbing the throat and then nose twice-weekly when attending work.

Sample storage/transport: 1 mL of liquid amies (MWE, UK). NP samples were stored at -80 °C, until further analysis.

Timing of sample collection: Twice per week during 12-week study period; not clearly related to symptoms but taken as part of surveillance

NAT extraction method: Genetic target: Quick DNA/RNA™ viral 142 MagBead kit (Zymo, USA)

Assay used: Genesig® Real-150 Time Coronavirus COVID-19 PCR assay (Genesig, UK)

Genetic target: NS

Threshold: Ct value < 40

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Saliva drool

Sample collection device: sterile tube (SARSTEDT, USA)

Sample collected by: Unsupervised patient

Sample collection method: Saliva (at least 500 µl) was collected once per week into a sterile tube (SARSTEDT, USA) by passive drool using a plastic funnel at home.

Sample storage/transport: Dry/direct sampling. Participants were asked to store saliva samples in their home freezers (approximately -20 °C) before transportation in cooler packs (provided by the research team) to the Liverpool School of Tropical Medicine (LSTM) laboratories for processing at monthly intervals.

Timing of sample collection: As for reference sample

NAT extraction method: QIAamp Viral 143 RNA Mini Kit (Qiagen, Germany)

Walker 2021 (Continued)

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: Liverpool COVID-19 Partnership Strategic Research Fund to NFW

Publication status: Pre-print

Source: MedRxiv

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Was the intention that patients receive all tests at all time points?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
If a threshold was used, was it pre-specified?	Yes		

Walker 2021 (Continued)

Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	No
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	High risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes
If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	No
Were the proportions and reasons for missing data similar across sample types (index test)?	Unclear

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Walker 2021 (Continued)

Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	High risk

Wang 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP and OP samples for the diagnosis of COVID-19 Design: 353 (76) participants with paired nasopharyngeal and oropharyngeal swabs for diagnosis of SARS-CoV-2 by RT-PCR, including both outpatients (admitted to fever clinic due to COVID-19-like symptoms and fever or chest X-ray abnormality), (n = 192) and inpatients (hospital designated for severe and very severe COVID-19 patients), (n = 161) Recruitment: Unclear; "We reviewed the medical records from February 16, 2020 to March 2, 2020, and compared the performance between nasopharyngeal and oropharyngeal swabs in SARS-CoV-2 detection from 353 patients who received tests with both specimens simultaneously." Prospective or retrospective: Retrospective
Patient characteristics and setting	Setting: Mixed Location: Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China Country: China Dates: From February 16, 2020 to March 2, 2020 Symptoms and severity: Outpatient (fever clinic) 192 (19, 9.9%) Inpatient 161 (57, 35.4%) Demographics: Whole cohort: Median age 54 y (IQR 39 to 65, range 20 to 88) Sex: 176, 50% male Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: Not stated Sample collection method: swab from single nostril; Quote: "swab was collected from single nostril according to a detailed video in a previously published study (Baden 2009)" Sample storage/transport: Stored in a collection tube with 5 mL virus preservation solution Timing of sample collection: Outpatients: infer at first healthcare contact Inpatients: Unclear NAAT extraction method: RNA was isolated with Tianlong PANA9600 automatic nucleic acid extraction system (Tianlong, Xi'an, China).

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Wang 2020 (Continued)

Assay used: RT-PCR (DAAN GENE; Guangzhou, China)

Genetic target: N, ORF1ab

Threshold: Ct < 40 for both genes defined as positive

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample: Oropharyngeal (OP)

Sample collected by: Not stated

Sample collection method: "A oropharyngeal swab was collected from both sides of the throat according to a published video by Chinese Society of Laboratory Medicine ([Baden 2009](#))."

Sample storage/transport: As for reference sample

Timing of sample collection: As for reference sample

NAAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Unclear, probably no

Time interval between sampling methods: Simultaneous

All patients received all sampling methods: Yes

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: This study was supported by National Mega Project on Major Infectious Disease Prevention (No. 2017ZX10103005-007 for Ziyong Sun) and National Key Research and Development Program of China (No. 2018YFE0204500for Weiyong Liu).

Publication status: Published paper

Source: Academic journal

Author COI: The authors declared that they had no conflict of interest.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns

Wang 2020 (Continued)

DOMAIN 1: Patient selection

Was a consecutive or random sample of patients enrolled? Unclear

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Unclear

Did the study avoid inappropriate inclusions? Unclear

Was the intention that patients receive all tests at all time points? Unclear

Could the selection of patients have introduced bias? Unclear risk

Are there concerns that the included patients and setting do not match the review question? Unclear

DOMAIN 2: Index test (Saliva)
DOMAIN 2: Index test (Gargle)
DOMAIN 2: Index test (Oral swab)
DOMAIN 2: Index test (Oropharyngeal)

If a threshold was used, was it pre-specified? Yes

Is undergoing one sample type unlikely to influence the result of the other sample type? Unclear

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types? Yes

If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern

DOMAIN 2: Index test (Collection method)
DOMAIN 2: Index test (Oropharyngeal/nasal)
DOMAIN 2: Index test (Nasal)
DOMAIN 2: Index test (Oral rinse)
The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

Wang 2020 (Continued)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? Unclear risk

Wehrhahn 2020

Study characteristics

Patient Sampling	Single-group study to estimate agreement between NP/OP and OP, nasal mid-turbinate and OP/nasal mid-turbinate samples for the diagnosis of COVID-19 Design: 166 (13) patients presenting for SARS-CoV-2 testing at dedicated COVID-19 testing sites <i>1 of 2 sites contributing data excluded from this review (n = 70) because of an average of 2.5 days between collection of samples for comparison.</i> Recruitment: Unclear, probably consecutive: "For a period of one week in March 2020, patients presenting ... were offered participation in the study..." Prospective or retrospective: Prospective Additional inclusion criteria: '24 patients recently diagnosed with COVID-19' contributed to data but 'n' not reported; unclear if these patients were diagnosed on the basis of one of more samples and unclear whether this was one or both sites.
Patient characteristics and setting	Setting: Outpatient/community; COVID-19 testing clinics and own homes

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Wehrhahn 2020 (Continued)

Location: Not stated; Author institution laboratories were: Douglass Han-ly Moir Pathology, Macquarie Park NSW, and Sullivan Nicolaides Pathology, Bowen Hills, QLD

Country: Australia

Dates: One week in March 2020

Symptoms and severity: 'symptomatic ambulatory patients'

Demographics: Across 2 sites (n = 236):

Median age 40 (range 9–81) years

Sex: 94 (40%) male.

Exposure history: Not stated

Index tests

Reference Sample: Naso/oropharyngeal (NP/OP)

Sample collected by: HCW

Sample collection method: flocked NP swab and a foam throat swab

Sample storage/transport: Not described

Timing of sample collection: Cases: mean 4.8 days (range 2 to 9 days) pso

NAAT extraction method: MagNA Pure 96 (Roche, Basel, Switzerland)

Assay used: RT-PCR; in-house (Taqman assay)

Genetic target: E gene

Threshold: ≤ 40 Ct

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample [A]:

Combined index sample [B] & [C]

Index Sample [B]: Nasal mid-turbinate

Sample collected by: Patient

Sample collection method: open-cell polyurethane foam swabs (Σ Transwab[®] ref MW940, Medical Wire & Equipment (MWE), Wiltshire, England); self-col-lection kits included two swab packets each containing a single swab and screw-top container with 2 mL liquid Amies medium. Nasal swabs were in-serted 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.

Sample storage/transport: In separate containers per swab with 2 mL liquid Amies medium

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Wehrhahn 2020 (Continued)

Blinding reported: Not stated

Threshold predefined: Yes

Index Sample [C]: Oropharyngeal (OP)

Sample collected by: Patient

Sample collection method: open-cell polyurethane foam swabs (Σ Transwab® ref MW940, Medical Wire & Equipment (MWE), Wiltshire, England); self-collection kits included two swab packets each containing a single swab and screw-top container with 2 mL liquid Amies medium. Throat swabs were collected from the posterior throat and tonsil areas.

Sample storage/transport: In separate containers per swab with 2 mL liquid Amies medium

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: Not stated

Threshold predefined: Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Yes; self-collected samples were taken immediately prior to trained HCW-collected samples to reduce 'training bias.' Throat swabs obtained prior to nasal swabs

Time interval between sampling methods: Simultaneous
All patients received all sampling methods: Yes, at included site

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Publication status: Published paper

Source: Journal of Clinical Virology

Author COI: The authors declared that they had no competing interests.

Methodological quality

Item

Authors' judgement

Risk of bias

Applicability concerns

DOMAIN 1: Patient selection

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Wehrhahn 2020 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Unclear
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Unclear
Was the intention that patients receive all tests at all time points?	Yes
Could the selection of patients have introduced bias?	Unclear risk
Are there concerns that the included patients and setting do not match the review question?	High
DOMAIN 2: Index test (Saliva)	
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Yes
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear

Wehrhahn 2020 (Continued)

Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Nasal)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	
DOMAIN 3: Reference standard	
Could the reference standard, its conduct, or its interpretation have introduced bias?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	
DOMAIN 4: Flow and timing	
Was there an appropriate interval between index tests?	Yes

Wehrhahn 2020 (Continued)

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point	Yes
Were the proportions and reasons for missing data similar across sample types (index test)?	Yes
Were results presented per patient?	Yes
Were all patients included in the analysis?	Unclear
Could the patient flow have introduced bias?	Unclear risk

Williams 2020

Study characteristics

Patient Sampling	Study aim: Two-group study to compare estimate agreement between NP and saliva samples for the diagnosis of COVID-19 Design: 89 (40) patients presenting to a dedicated COVID-19 screening clinic Recruitment: Paired sample results reported for all positive NP samples and for a random sample of negative NP samples out of a total of 622 individuals Prospective or retrospective: Unclear; probably mixed
Patient characteristics and setting	Setting: Community/outpatient; ambulatory patients in screening clinic Location: Royal Melbourne Hospital (RMH), Melbourne Country: Australia Dates: 25th March to 1st April 2020 Symptoms and severity: Not stated Demographics: Not stated Exposure history: Not stated
Index tests	Reference Sample: Nasopharyngeal (NP) Sample collected by: Not stated; presume HCW Sample collection method: swab; no further details (use of VTM not reported) Sample storage/transport: The median time from sample collection to addition of media was 180 minutes (range 55–537 minutes). Timing of sample collection: Range 0 to 21 (from figure 2); most days 10 or less pso NAAT extraction method: Qiagen EZ1 platform (QIAGEN, Hilden, Germany), using extraction volume of 200 uL of sample, with RNA eluted in 60 uL Assay used: Multiplex RT-PCR test for SARS-CoV-2 and other seasonal coronaviruses (Coronavirus Typing (8-well) assay, AusDiagnostics, Mascot, Australia) Genetic target: Not stated

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Williams 2020 (Continued)

Threshold: Not stated; all NP+ samples for SARS-CoV-2 underwent confirmatory testing at a local reference laboratory (the Victorian Infectious Diseases Reference Laboratory) using previously published primers.

Blinding reported: Not stated

Threshold predefined: Not stated; presume Yes

Index Sample: Saliva

Sample collection device: Not stated

Sample collected by: Self-collection

Sample 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 25 mL collection pot.

Sample storage/transport: Transported neat; approximate 1:1 ratio of liquid Amies media added

Timing of sample collection: Range 0 to 21 (from figure 2)

NAT extraction method: as for sampling method A

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: Not stated

Blinding reported: Not stated

Threshold predefined: Not stated; presume Yes

Target condition and reference standard(s)

Flow and timing

Sampling schedule prespecified: Not stated

Time interval between sampling methods: Simultaneous
All patients received all sampling methods: Unclear, 522/622 had saliva samples and unclear how many saliva samples had RT-PCR

Missing data: None reported

Uninterpretable results: None reported

Indeterminate results: None reported

Comparative

Notes

Funding: No funding statement provided

Publication status: Published paper

Source: Journal of Clinical Microbiology

Author COI: The authors declared that they had no conflict of interest.

Methodological quality

Item
Authors' judgement
Risk of bias
Applicability concerns

DOMAIN 1: Patient selection

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Williams 2020 (Continued)

Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Unclear
Did the study avoid inappropriate inclusions?	Yes
Was the intention that patients receive all tests at all time points?	Unclear
Could the selection of patients have introduced bias?	High risk
Are there concerns that the included patients and setting do not match the review question?	Low concern
DOMAIN 2: Index test (Saliva)	
If a threshold was used, was it pre-specified?	Yes
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes
If patients underwent multiple sample types, was the test result from one sample type interpreted without knowledge of the test result from the other sample type?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern
DOMAIN 2: Index test (Gargle)	
DOMAIN 2: Index test (Oral swab)	
DOMAIN 2: Index test (Oropharyngeal)	
DOMAIN 2: Index test (Collection method)	
DOMAIN 2: Index test (Oropharyngeal/nasal)	
DOMAIN 2: Index test (Nasal)	
DOMAIN 2: Index test (Oral rinse)	
DOMAIN 2: Index test (Operator)	

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Williams 2020 (Continued)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point No

Were the proportions and reasons for missing data similar across sample types (index test)? No

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias? High risk

Zander 2021
Study characteristics

Patient Sampling	Design: Close contacts of SARS-CoV-2-positive persons traced by health authorities (n = 80). Most symptomatic at the time of testing Recruitment: Unclear. Between October and December 2020 Prospective or retrospective: Prospective Sample size (cases): 80 (26) Additional inclusion criteria: None
Patient characteristics and setting	Setting: Contact tracing Location: Different doctor's offices: Labor Dr. Brunner, Konstanz Praxis Dr. S. Scholtes/C. Zeleny, Konstanz Praxis Maximilian Ottinger, Konstanz Country: Germany Dates: Between October and December 2020 Symptoms and severity: ≥ 73% symptomatic in RT-PCR +ve; ≥ 69% symptomatic in RT-PCR -ve

Zander 2021 (Continued)

Demographics:

For RT-PCR positive:

Sex: 11/26 (42%) male

Age: median 33 (18-89)

For RT-PCR negative:

Sex: 21/54 (39%) male

Age: median 30 (13-77)

Exposure history: 80/80 (100%) with known exposure to COVID-19 case, traced by health authorities

Index tests

Reference sample: NP swab

Sample collection device: Copan eSwab with 1 mL Amies preservation medium

Sample collected by: HCW-collected/laboratory staff-interpreted

Sample collection method: Collection and container: NP swabs taken by professional medical staff in Copan eSwab (Copan; MAST Group) with 1 mL Amies preservation medium (APM)

Sample storage/transport: Amies preservation medium (APM)

Timing of sample collection: First Health Care contact as part of contact tracing

NAT extraction method: QIAcube HT, Qiagen

Assay used: Rida Gene SARS-CoV-2 assay (R-Biopharm) according to manufacturer's instructions

Genetic target: E gene

Threshold: The reporter emits a fluorescent signal that is detected by the optical unit of a real-time PCR device.

> 30Cq ('n = 4 positives had Cq > 30')

Blinding reported: NS

Threshold predefined: Yes

Index Sample: Gargle lavage fluid

Sample collection device: Not stated

Sample collected by: Patient-collected/laboratory staff-interpreted

Sample collection method: Collection: performed by gargling for 30 s with 5 mL of 0.9% saline for 30 s

Sample storage/transport: Sterile saline

Timing of sample collection: As for reference sample

NAT extraction method: As for reference sample

Assay used: As for reference sample

Genetic target: As for reference sample

Threshold: As for reference sample

Blinding reported: As for reference sample

Threshold predefined: As for reference sample

Zander 2021 (Continued)

Target condition and reference standard(s)

Flow and timing

Simultaneous sample collection: Yes

Missing data: Not stated

Uninterpretable results: Not stated

Indeterminate results: Not stated

Comparative

Notes

Funding: No funding

Publication status: Published paper

Source: Microbiology Spectrum

Author COI: Authors declared no COI present.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Was the intention that patients receive all tests at all time points?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index test (Saliva)			
DOMAIN 2: Index test (Gargle)			
If a threshold was used, was it pre-specified?	Yes		
Is undergoing one sample type unlikely to influence the result of the other sample type?	Unclear		
Were differences in the conduct or interpretation of tests for each sample type unlikely to advantage one of the sample types?	Yes		
If patients underwent multiple sample types, was the test result from one sample type interpreted	Unclear		

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Zander 2021 (Continued)

without knowledge of the test result from the other sample type?

Could the conduct or interpretation of the index test have introduced bias?

Unclear risk

Are there concerns that the index test, its conduct, or interpretation differ from the review question?

Low concern

DOMAIN 2: Index test (Oral swab)

DOMAIN 2: Index test (Oropharyngeal)

DOMAIN 2: Index test (Collection method)

DOMAIN 2: Index test (Oropharyngeal/nasal)

DOMAIN 2: Index test (Nasal)

DOMAIN 2: Index test (Oral rinse)

DOMAIN 2: Index test (Operator)

DOMAIN 3: Reference standard

Could the reference standard, its conduct, or its interpretation have introduced bias?

Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: Flow and timing

Was there an appropriate interval between index tests? Yes

If multiple samples were taken from individual patients (for example on day 1 and day 2 after symptoms onset), did all patients receive all index tests (samples, different collection methods) at each time point Yes

Were the proportions and reasons for missing data similar across sample types (index test)? Yes

Were results presented per patient? Yes

Were all patients included in the analysis? Unclear

Could the patient flow have introduced bias?

Unclear risk

Ag: antigen

AgRDT: Antigen Rapid Diagnostic Test

Ant: anterior

APM: Application Performance Management

ARI: acute respiratory infection
BD: twice per day
CDC: Centres for Disease Control
CGIA: Concentration Gradient Immunoassay
COI: conflict of interest
COVID-19: coronavirus disease-19
Cq: quantification cycle
Ct/CT: cycle threshold
CTAB: Cetyltrimethylammonium bromide
D+: Disease-positive
DHA: docosahexaenoic acid
DNA: deoxyribonucleic acid
ED: Emergency Department
EUA: Emergency Use Authorisation
FAM: 6-carboxyfluorescein
FN: false negative
FP: false positive
GEE: generalised estimating equation
GTC: guanidine thiocyanate
HCP: healthcare professional
HCW: healthcare worker
ICU: intensive care unit
IFU: instructions for use
IgA: Immunoglobulin A
IGI: Immunoglobulin I
IQR: interquartile range
LOD: limit of detection
LDT: laboratory developed test
MSKCC: Memorial Sloan Kettering Cancer Centre
MSU: Michigan State University
MT: mid-turbinate
MTM: Molecular Transport Medium
NAAT/NAT: Nucleic Acid Amplification Test
NaCl: sodium
NP: nasopharyngeal
NPA: negative per cent agreement
N-MT: nasal-mid-turbinate
N-Ant: nasal-anterior
NOS/nos: not otherwise specified
NP/OP: nasopharyngeal-orpharyngeal mixed swab
NPS: nasopharyngeal swab
NP-MT: Nasopharyngeal-Mid-Turbinate
NR: not reported
NS: not stated
ONPS: OroNasoPharyngeal Sample
ONS: oropharyngeal/nasal combined swab
OP: oropharyngeal
ORF(1ab): open reading frame 1ab
OS: oral sample
PBS: Phosphate buffer solution
PCR: polymerase chain reaction
PPA: per cent positive agreement
pso: particle swarm optimisation
RBC: red blood cell
RdRp: RNA-dependent RNA polymerase
RDT: Rapid Diagnostic Test
RNA: ribonucleic acid
RNase: ribonuclease
RT-PCR: reverse transcription polymerase chain reaction
RT-qPCR: Reverse Transcriptase quantitative Polymerase Chain REaction
Sars-CoV-2: severe acute respiratory syndrome coronavirus 2
SD: standard deviation

SOC: Standard Of Care
 TMA: transcription-mediated amplification
 UCSD: University of California San Diego
 USA: United States of America
 UTM: universal transport medium
 UVT: universal viral transport medium
 VoC: Variants of Concern
 VTM: viral transport medium
 WHO: World Health Organisation
 y: years
 -ve: negative
 +ve: positive

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Alghounaim 2020	Ineligible study design
Altamirano 2020	No paired samples
Avaniss-Aghajani 2020	Population preselected
Azzi 2020	Population preselected
Basso 2020	Accuracy data could not be extracted
Begum 2022a	Ineligible study design
Bennett 2020	Population preselected
Berenger 2020	Population preselected
Berenger 2021	No paired samples
Bergevin 2021	Ineligible target condition
Beyene 2021	Population preselected
Bland 2021	Accuracy data could not be extracted
Bloom 2021	No paired samples
Braz-Silva 2020	Conference abstract
Brotons 2020	Population preselected
Bulfoni 2021	Population preselected
Bulfoni 2022	Population preselected
Bundgaard 2021	No paired samples
Byrne 2020	Ineligible target condition
Calame 2020	Population preselected

Study	Reason for exclusion
Callahan 2020	Population preselected
Carmagnola 2021	Ineligible study design
Carvalho 2021	Ineligible study design
Casati 2021	Ineligible study design
Cassinari 2021	Accuracy data could not be extracted
Caulley 2020	Ineligible index test
Chan 2020a	No paired samples
Chan 2020b	Ineligible reference standard
Chapleau 2020	Ineligible study design
Chen 2020	Population preselected
Cheuk 2020	Population preselected
Chivte 2021	Ineligible reference standard
Chong 2020	Population preselected
Chotimah 2022	No paired samples
Chu 2021	No paired samples
Clementino 2022	Ineligible study design
Comerlato 2022	Population preselected
Connor 2022	Ineligible reference standard
Costa 2021	Population preselected
Costeloe 2021	Ineligible target condition
D'Andrea 2021	Population preselected
De Ioris 2020	Population preselected
Delaney 2020	No paired samples
De Marinis 2021	Ineligible study design
De Marinis 2021a	Population preselected
De Oliveira 2022	Accuracy data could not be extracted
De Santi 2021	Ineligible study design
Dhakad 2021	Ineligible study design

Study	Reason for exclusion
Di Pietro 2020	Ineligible study design
Donato 2021	Population preselected
Esteves 2022	Population preselected
Fabiani 2022	Ineligible index test
Fan 2020	Population preselected
Fang 2020	Population preselected
Federman 2020	Population preselected
Fougere 2021a	Accuracy data could not be extracted
Fowler 2020	No paired samples
Freire-Paspuel 2020	Ineligible reference standard
Fronza 2022	Conference abstract
Gable 2021	Population preselected
Gan 2020	Population preselected
Georgas 2022	No paired samples
Girish 2021	Ineligible study design
Goldfarb 2020	No paired samples
Goodall 2022	No paired samples
Green 2020	No paired samples
Grijalva 2020	Population preselected
Guo 2020	Population preselected
Guthrie 2020	Population preselected
Guthrie 2021	No paired samples
Hagbom 2021	Ineligible study design
Hamed 2020	Ineligible study design
Han 2020	Population preselected
He 2020	Population preselected
Hernandez 2021	Ineligible study design
Hitzenbichler 2021	Ineligible reference standard

Study	Reason for exclusion
Ho 2021	Population preselected
Hoch 2021	Population preselected
Hofman 2021	No paired samples
Homza 2021	Population preselected
Hu 2020	Ineligible study design
Iftner 2022	Ineligible index test
Igloi 2021	Population preselected
Iwasaki 2020	Population preselected
Jamal 2020	Population preselected
Jayaprakasam 2021	Ineligible reference standard
Jiang 2020	Population preselected
Kalil 2021	Ineligible index test
Kandel 2020	No paired samples
Kandel 2021	Ineligible index test
Kerimov 2021	Population preselected
Kidd 2022	No paired samples
Kim 2020	Ineligible index test
Kim 2020a	Population preselected
Kim 2022	Ineligible study design
Kinshella 2022	Population preselected
Kitt 2020	Population preselected
Kiyasu 2021	Ineligible study design
Kiyasu 2022	Ineligible reference standard
Kiyasu 2022a	Population preselected
Klein 2021a	Ineligible study design
Kobayashi 2021	No paired samples
Kojima 2021	No paired samples
Kritikos 2021	Ineligible reference standard

Study	Reason for exclusion
Kujawski 2020	Population preselected
Kwon 2021	No paired samples
Lai 2020	Population preselected
Lai 2021	Accuracy data could not be extracted
Lalli 2021	Population preselected
Landaverde 2022	No paired samples
Lapierre 2021	Accuracy data could not be extracted
LeBlanc 2020	No paired samples
LeBlanc 2021	Ineligible study design
Levican-Asenjo 2020	Population preselected
Li 2020	Population preselected
Lin 2020	Accuracy data could not be extracted
Lin 2022	Ineligible reference standard
Lindner 2021a	Ineligible study design
Lindner 2021b	Ineligible target condition
Lindner 2021c	Population preselected
Lopez-Martinez 2020	Accuracy data could not be extracted
Lu 2020	No paired samples
Lui 2020	Population preselected
Lyu 2020	Population preselected
L'Helgouach 2020	Ineligible study design
Mahmood 2021	Ineligible reference standard
Mak 2022	Ineligible study design
Malczynski 2020	Ineligible index test
Manzoor 2020	No paired samples
Masia 2021	No paired samples
Masse 2021	Ineligible study design
Matic 2020	No paired samples

Study	Reason for exclusion
Matic 2020a	No paired samples
Michalina 2022	Population preselected
Miller 2022	Ineligible study design
Miranda-Ortiz 2021	Ineligible reference standard
Mittal 2020	Population preselected
Mollaei 2020	No paired samples
Montano 2022	Population preselected
Moore 2020a	Population preselected
Naito 2021	Accuracy data could not be extracted
Nikolai 2021	Ineligible study design
Oba 2022	No paired samples
Onsongo 2022	Population preselected
Paap 2022	Ineligible study design
Paliksa 2021	Ineligible study design
Palmas 2020	Population preselected
Pan 2020	Population preselected
Peng 2020	Population preselected
Perkins 2022	No paired samples
Phan 2022	No paired samples
Pinninti 2020	Population preselected
Qiu 2022	No paired samples
Radbel 2020	Population preselected
Rao 2020a	Population preselected
Rao 2020b	Population preselected
Ren 2021	No paired samples
Ricci 2021	Ineligible reference standard
Robinson 2022	No paired samples
Sarinoglu 2021	Ineligible target condition

Study	Reason for exclusion
Sasikala 2021	No paired samples
Savage 2021	Population preselected
Sawano 2021	Ineligible index test
Schrom 2022	Ineligible study design
Schuit 2021	No paired samples
Singh 2021	Ineligible reference standard
Suh 2021	Ineligible study design
Sun 2021	Population preselected
Sutjipto 2020	Population preselected
Takeuchi 2021	Accuracy data could not be extracted
Taki 2021	Ineligible study design
Tallmadge 2021	No paired samples
Tan 2020	Population preselected
Tang 2020	Population preselected
Ter-Ovanesyan 2021a	Ineligible study design
Ter-Ovanesyan 2021b	No paired samples
Therchilsen 2020	Population preselected
Thwe 2021	Ineligible study design
To 2020	No paired samples
Trobajo-Sanmartin 2021	No paired samples
Truong 2020	Accuracy data could not be extracted
Truong 2021	Ineligible study design
Unsalier 2021	Ineligible reference standard
Uribe-Alvarez 2021	No paired samples
Uwamino 2020	Population preselected
Vander 2021	No paired samples
Venekamp 2021	No paired samples
Villota 2021	Ineligible study design

Study	Reason for exclusion
Vogels 2021	No paired samples
Wang 2020a	Population preselected
Wei 2020	No paired samples
Wolfl-Duchek 2022	Ineligible study design
Won 2021	Ineligible study design
Wong 2021	Ineligible study design
Woodall 2021	Population preselected
Wu 2020a	No paired samples
Wu 2020b	Ineligible study design
Wyllie 2020	Population preselected
Wyllie 2022	Population preselected
Xiao 2020	Population preselected
Xie 2020	Ineligible study design
Xu 2020	Population preselected
Ye 2020 (a)	Ineligible study design
Yin 2022	No paired samples
Yokota 2021	Population preselected
Young 2020	Ineligible study design
Yu 2020	Population preselected
Yuan 2020	No paired samples
Zhang 2022	Ineligible study design
Zheng 2020	Population preselected
Zobrist 2022	Population preselected

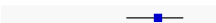
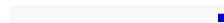
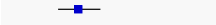
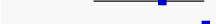
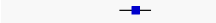
DATA

Presented below are all the data for all of the tests entered into the review.

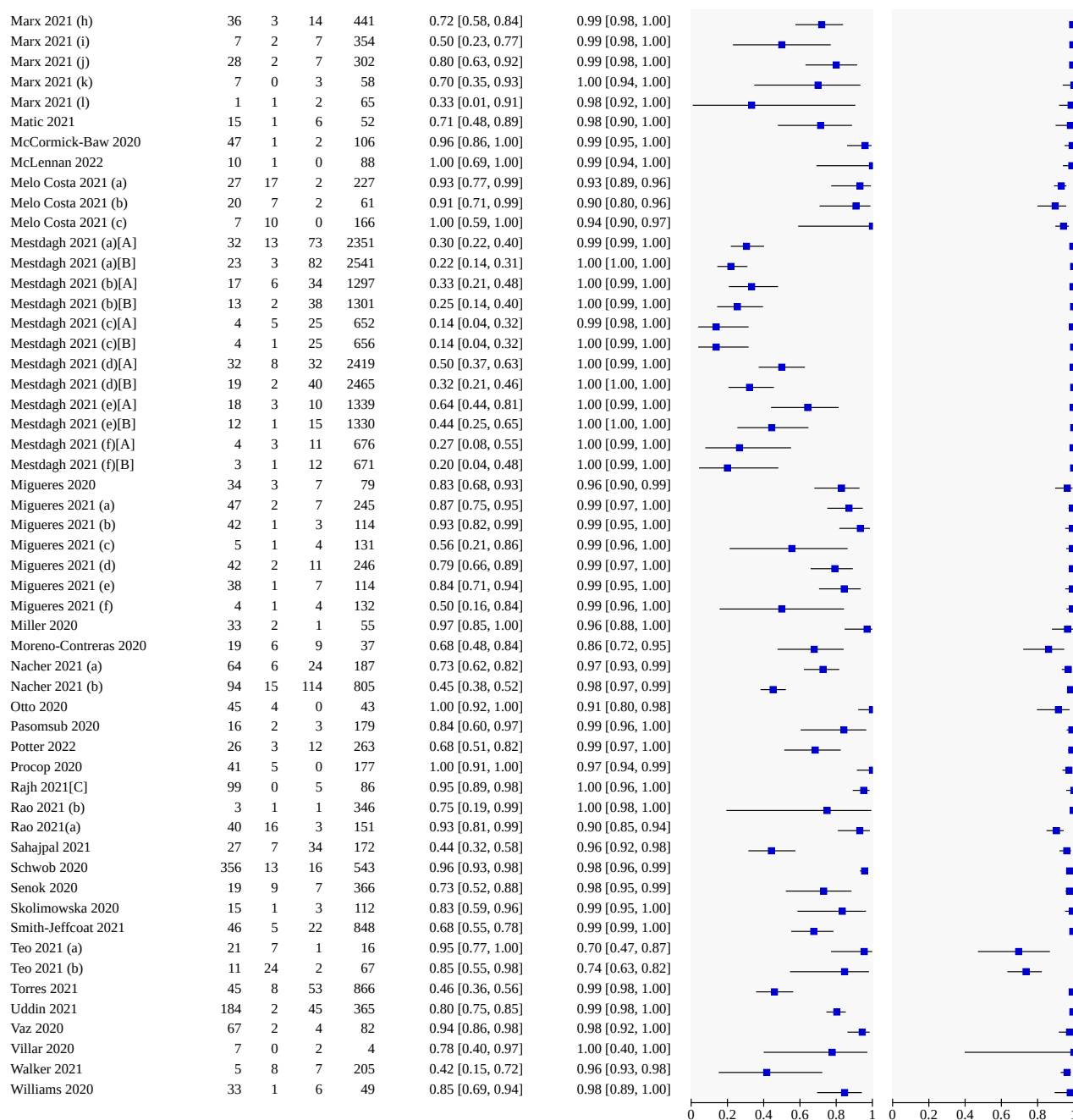
Table Tests. Data tables by test

Test	No. of studies	No. of participants
1 Saliva	120	55444
2 Oral rinse	2	238
3 Gargle	6	2138
4 All nasal (mid-turbinate, anterior and nos)	44	14985
5 Oropharyngeal (OP)	7	2522
6 Nasal/OP	4	701
7 Oral swab	4	1243
8 Operator	4	360

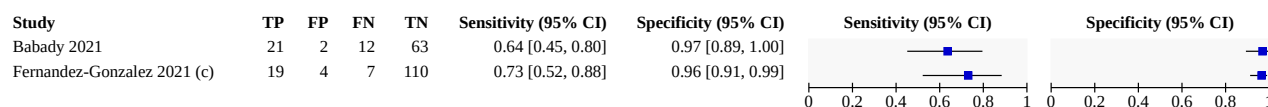
Test 1. Saliva

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
AbdulRahman 2020a	35	12	13	949	0.73 [0.58, 0.85]	0.99 [0.98, 0.99]		
AbdulRahman 2020b	13	2	2	70	0.87 [0.60, 0.98]	0.97 [0.90, 1.00]		
Aita 2020	0	0	0	326	Not estimable	1.00 [0.99, 1.00]		
Akgun Dogan 2021	35	1	63	101	0.36 [0.26, 0.46]	0.99 [0.95, 1.00]		
Al Suwaidi 2021	64	6	10	396	0.86 [0.77, 0.93]	0.99 [0.97, 0.99]		
Altawalah 2020	287	18	57	527	0.83 [0.79, 0.87]	0.97 [0.95, 0.98]		
Babady 2021	16	1	1	69	0.94 [0.71, 1.00]	0.99 [0.92, 1.00]		
Banerjee 2021	53	2	4	51	0.93 [0.83, 0.98]	0.96 [0.87, 1.00]		
Becker 2020	11	2	10	62	0.52 [0.30, 0.74]	0.97 [0.89, 1.00]		
Bhattacharya 2021	53	0	5	16	0.91 [0.81, 0.97]	1.00 [0.79, 1.00]		
Bidkar 2022	15	3	30	32	0.33 [0.20, 0.49]	0.91 [0.77, 0.98]		
Bikos 2021	58	5	7	173	0.89 [0.79, 0.96]	0.97 [0.94, 0.99]		
Boerger 2021	28	2	2	244	0.93 [0.78, 0.99]	0.99 [0.97, 1.00]		
Borghi 2021a	59	1	27	105	0.69 [0.58, 0.78]	0.99 [0.95, 1.00]		
Borghi 2021b	9	0	3	68	0.75 [0.43, 0.95]	1.00 [0.95, 1.00]		
Borghi 2021c	20	6	1	82	0.95 [0.76, 1.00]	0.93 [0.86, 0.97]		
Boutros 2021 (b)	41	0	16	205	0.72 [0.58, 0.83]	1.00 [0.98, 1.00]		
Boutros 2021(a)	54	1	4	88	0.93 [0.83, 0.98]	0.99 [0.94, 1.00]		
Bruxvoort 2021	291	0	37	1784	0.89 [0.85, 0.92]	1.00 [1.00, 1.00]		
Callahan 2021(e)	59	5	4	275	0.94 [0.85, 0.98]	0.98 [0.96, 0.99]		
Castelain 2021	2	0	24	475	0.08 [0.01, 0.25]	1.00 [0.99, 1.00]		
Chu 2021 (a)	17	4	16	263	0.52 [0.34, 0.69]	0.99 [0.96, 1.00]		
Chu 2021 (b)	29	1	11	66	0.72 [0.56, 0.85]	0.99 [0.92, 1.00]		
Congrave-Wilson 2021	258	60	266	305	0.49 [0.45, 0.54]	0.84 [0.79, 0.87]		
Da Costa Fernandes 2021	60	0	16	16	0.79 [0.68, 0.87]	1.00 [0.79, 1.00]		
Da Silva 2022	15	3	1	42	0.94 [0.70, 1.00]	0.93 [0.82, 0.99]		
De Oliveira 2021	119	5	33	243	0.78 [0.71, 0.85]	0.98 [0.95, 0.99]		
Desai 2021(a)[C]	12	2	2	105	0.86 [0.57, 0.98]	0.98 [0.93, 1.00]		
Desai 2021(b)	110	54	66	923	0.63 [0.55, 0.70]	0.94 [0.93, 0.96]		
Echavarria 2021	61	1	2	110	0.97 [0.89, 1.00]	0.99 [0.95, 1.00]		
Escobar 2021	50	1	3	73	0.94 [0.84, 0.99]	0.99 [0.93, 1.00]		
Felix 2022	6	2	2	40	0.75 [0.35, 0.97]	0.95 [0.84, 0.99]		
Fernandez-Gonzalez 2021(a)	39	11	8	171	0.83 [0.69, 0.92]	0.94 [0.89, 0.97]		
Fernandez-Gonzalez 2021(b)	28	0	14	166	0.67 [0.50, 0.80]	1.00 [0.98, 1.00]		
Fernández-Pittol 2020	30	1	7	13	0.81 [0.65, 0.92]	0.93 [0.65, 1.00]		
Fougere 2021	86	5	15	291	0.85 [0.77, 0.91]	0.98 [0.96, 0.99]		
Fronza 2021 (a)	56	9	12	116	0.82 [0.71, 0.91]	0.93 [0.87, 0.97]		
Fronza 2021 (b)	15	0	0	17	1.00 [0.78, 1.00]	1.00 [0.80, 1.00]		
Goncalves 2021	55	7	23	122	0.71 [0.59, 0.80]	0.95 [0.89, 0.98]		
Griesemer 2021 (a)	6	0	6	224	0.50 [0.21, 0.79]	1.00 [0.98, 1.00]		
Griesemer 2021 (b)	79	2	12	134	0.87 [0.78, 0.93]	0.99 [0.95, 1.00]		
Guclu 2020 (a)	2	2	1	10	0.67 [0.09, 0.99]	0.83 [0.52, 0.98]		
Guclu 2020 (b)	26	2	4	17	0.87 [0.69, 0.96]	0.89 [0.67, 0.99]		
Guzman-Ortiz 2021	14	6	3	133	0.82 [0.57, 0.96]	0.96 [0.91, 0.98]		
Hamilton 2021	9	4	4	106	0.69 [0.39, 0.91]	0.96 [0.91, 0.99]		
Herrera 2021	150	22	68	1867	0.69 [0.62, 0.75]	0.99 [0.98, 0.99]		
Huber 2021 (a)	245	8	20	997	0.92 [0.89, 0.95]	0.99 [0.98, 1.00]		
Huber 2021 (b)	217	3	18	862	0.92 [0.88, 0.95]	1.00 [0.99, 1.00]		
Huber 2021 (c)	28	5	2	135	0.93 [0.78, 0.99]	0.96 [0.92, 0.99]		
Justo 2021	40	0	1	35	0.98 [0.87, 1.00]	1.00 [0.90, 1.00]		
Kannian 2021	44	2	11	23	0.80 [0.67, 0.90]	0.92 [0.74, 0.99]		
Kermeis 2021 (a)	105	12	7	1204	0.94 [0.88, 0.97]	0.99 [0.98, 0.99]		
Kermeis 2021 (b)	83	26	4	403	0.95 [0.89, 0.99]	0.94 [0.91, 0.96]		
Kermeis 2021 (c)	22	39	3	748	0.88 [0.69, 0.97]	0.95 [0.93, 0.96]		
Kojima 2020	20	6	3	16	0.87 [0.66, 0.97]	0.73 [0.50, 0.89]		
Landry 2020	28	2	5	89	0.85 [0.68, 0.95]	0.98 [0.92, 1.00]		

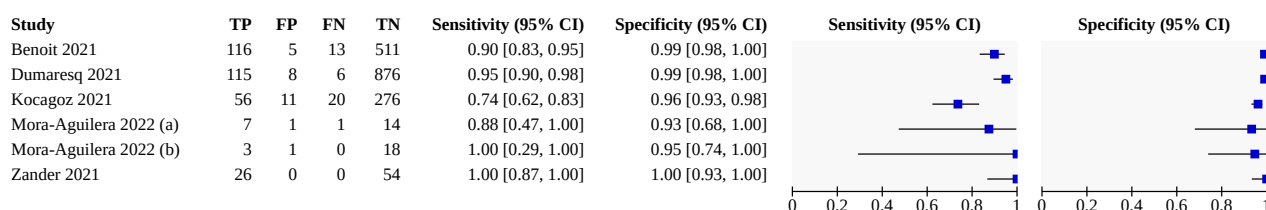
Test 1. (Continued)



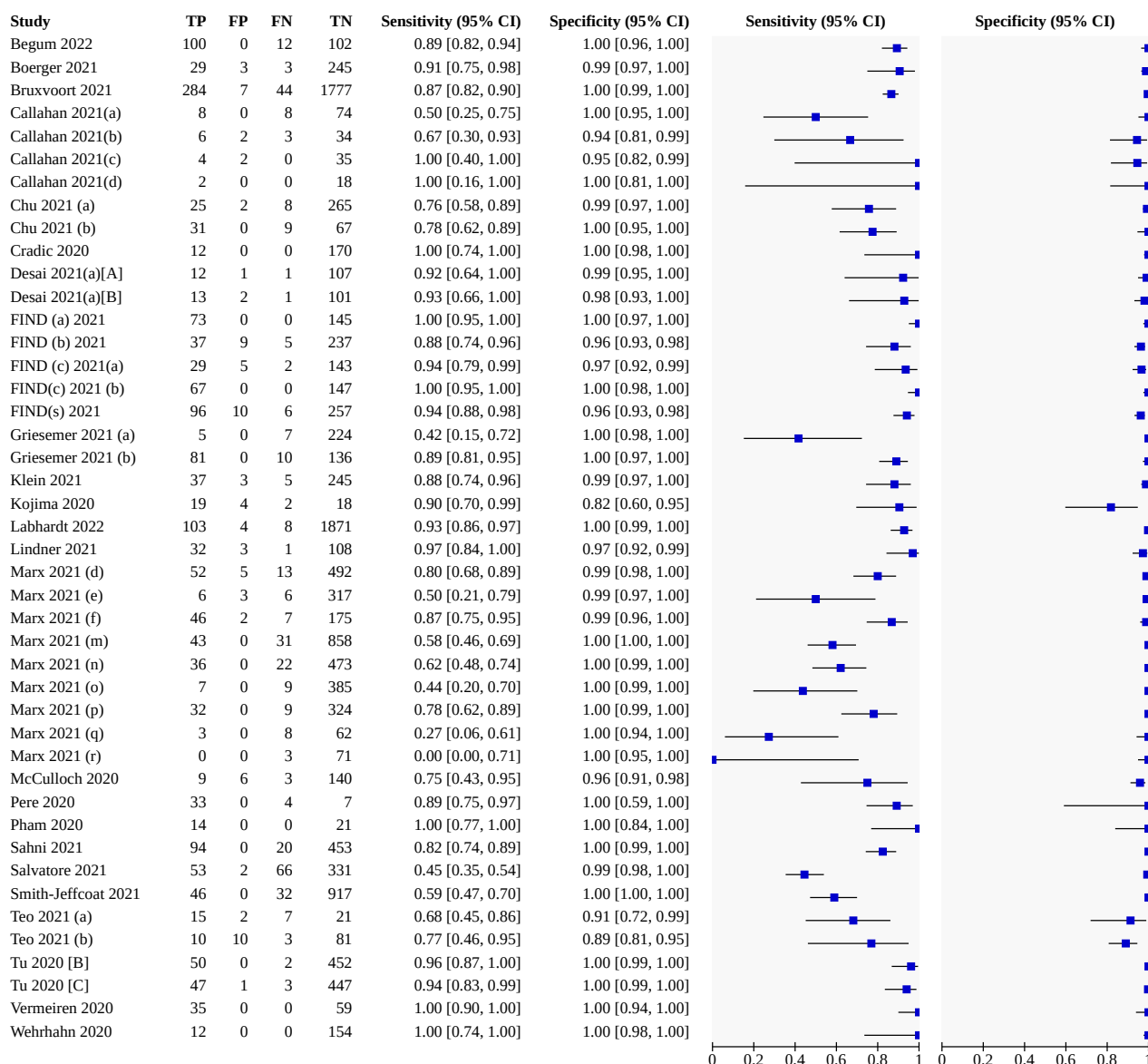
Test 2. Oral rinse



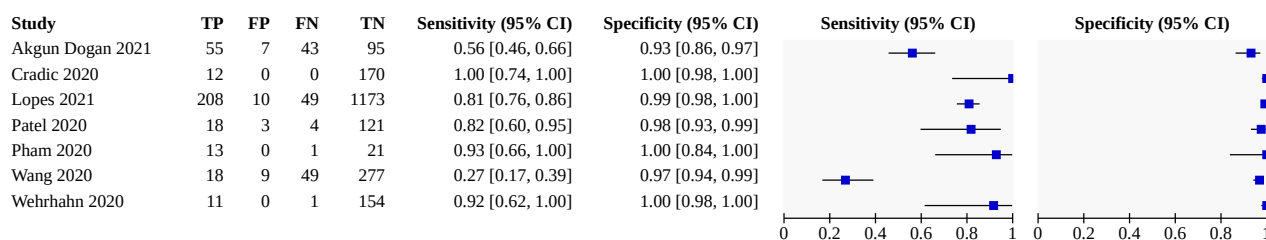
Test 3. Gargle



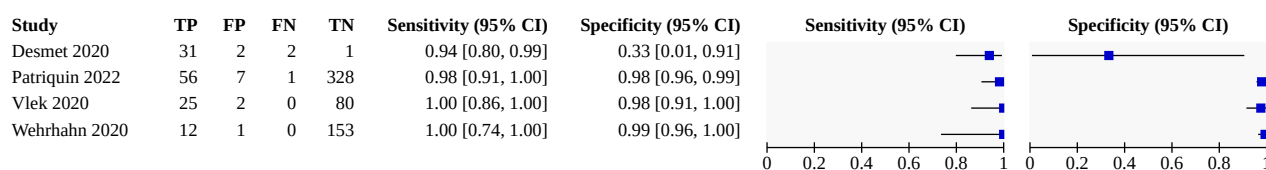
Test 4. All nasal (mid-turbinate, anterior and nos)



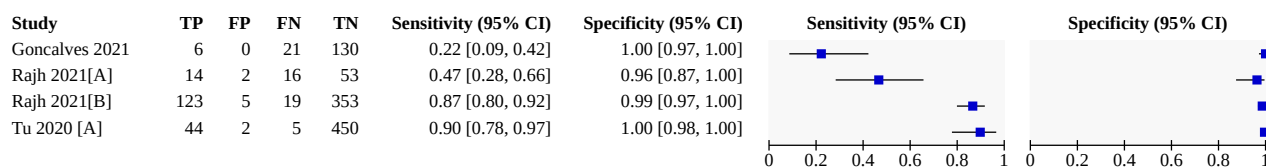
Test 5. Oropharyngeal (OP)



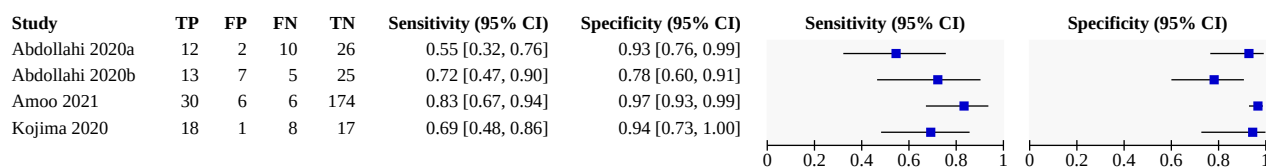
Test 6. Nasal/OP



Test 7. Oral swab



Test 8. Operator



ADDITIONAL TABLES

Table 1. Study findings summary tables: all anatomical sample types

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	Heterogeneity τ^2
Saliva	90 (89)*	40,342 (40,016)*	7341	-0.12 (-0.16 to -0.08)	< 0.0001	0.025
By COVID-19 test tech						
PCR	86 (85)*	38,657 (38,331)*	6980	-0.12 (-0.16 to -0.09)	< 0.0001	0.026

Table 1. Study findings summary tables: all anatomical sample types *(Continued)*

Isothermal	2	1274	246	-0.05 (-0.13 to 0.04)	0.305	0
TMA	2	411	115	-0.06 (-0.12 to 0.01)	0.088	0
<i>Difference across sub-groups</i>	-				0.797	-
By sample collection						
Deep throat	11	2192	730	0.10 (-0.01 to 0.21)	0.068	0.027
Drool	11	2325	683	-0.16 (-0.27 to -0.05)	0.005	0.028
Salivate	11 (10)*	7502 (7176)*	801	-0.21 (-0.37 to -0.05)	0.011	0.062
Spit	35	17752	3152	-0.13 (-0.18 to -0.08)	< 0.0001	0.018
Swab and drool	1	928	385	-0.01 (-0.04 to 0.02)	0.577	N/A
Not otherwise specified	21	9643	1590	-0.16 (-0.23 to -0.08)	< 0.0001	0.027
<i>Difference across sub-groups†</i>	-				0.008	-
Nasal	37	12,979	2020	-0.06 (-0.08 to -0.04)	< 0.0001	0.001
<i>By COVID-19 test tech</i>						
PCR + isothermal	29	9291	1485	-0.12 (-0.17 to -0.07)	< 0.0001	0.011
Rapid antigen test (Ag)	8	3688	535	0.00 (-0.002 to 0.002)	0.974	0
<i>Difference across sub-groups</i>	-				0.054	-
By sample collection						
Anterior	15	8272	998	-0.11 (-0.18 to -0.04)	0.002	0.013
Mid-turbinate	19	3942	786	-0.06 (-0.09 to -0.03)	< 0.0001	0.002
Not otherwise specified	3	765	236	-0.02 (-0.11 to 0.06)	0.547	0.004
<i>Difference across sub-groups†</i>	-				0.682	-
Oropharyngeal (OP)	7	2522	511	-0.17 (-0.29 to -0.05)	0.006	0.022
Gargle	6	2138	389	-0.01 (-0.05 to 0.02)	0.427	0.001
Nasal/OP	4	701	139	0.07 (0.01 to 0.12)	0.012	0
Oral rinse	2	238	65	-0.20 (-0.38 to -0.02)	0.030	0.007

Table 1. Study findings summary tables: all anatomical sample types *(Continued)*

Oral swab	4	1243	257	-0.33 (-0.62 to -0.05)	0.022	0.080

*Numbers in brackets are those included in calculating the pooled estimates.

†Comparison excluding 'not otherwise specified'

Abbreviations

Ag: antigen; CI: confidence interval; COVID-19: coronavirus disease 19; N/A: not applicable; PCR: polymerase chain reaction; RT-PCR: reverse transcription polymerase chain reaction; Tech: technology; TMA: transcription-mediated amplification

Table 2. Saliva: Numerical summary of evaluations

	Deep throat	Drool	Salivate	Spit	Swab and drool	Not otherwise specified	Total
Number of test evaluations	11	11	11	35	1	21	90
Number of sample pairs (participants) [Median (IQR)]	95 (51 to 223)	200 (123 to 236)	273 (147 to 596)	243 (131 to 595)	928	127 (76 to 501)	209 (99 to 409)
Number of COVID-19 cases [Median (IQR)]	38 (29 to 58)	59 (35 to 99)	59 (27 to 108)	58 (32 to 94)	385	54 (32 to 69)	56.5 (32 to 85)
Setting, n (%)							
Community	6 (54.6)	1 (9.1)	2 (18.2)	4 (11.4)	0 (0)	1 (4.8)	14 (15.6)
Contact tracing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
COVID-19 test centre	0 (0)	4 (36.4)	5 (45.5)	10 (28.6)	1 (100)	3 (14.3)	23 (25.6)
Inpatient	2 (18.2)	1 (9.1)	1 (9.1)	0 (0)	0 (0)	1 (4.8)	5 (5.6)
Mixed	0 (0)	1 (9.1)	0 (0)	9 (25.7)	0 (0)	4 (19.1)	14 (15.6)
Outpatient	2 (18.2)	2 (18.2)	0 (0)	9 (25.7)	0 (0)	7 (33.3)	20 (22.2)
Screening	1 (9.1)	1 (9.1)	0 (0)	0 (0)	0 (0)	2 (9.5)	4 (4.4)
Unclear	0 (0)	1 (9.1)	3 (27.3)	3 (8.6)	0 (0)	3 (14.3)	10 (11.1)
Age, n (%)							
Adult	9 (81.8)	4 (36.4)	7 (63.6)	15 (42.9)	1 (100)	13 (61.9)	49 (54.4)
Child	0 (0)	2 (18.2)	1 (9.1)	3 (8.6)	0 (0)	0 (0)	6 (6.7)
Mixed	0 (0)	3 (27.3)	1 (9.1)	11 (31.4)	0 (0)	2 (9.5)	17 (18.9)
Unclear	2 (18.2)	2 (18.2)	2 (18.2)	6 (17.1)	0 (0)	6 (28.6)	18 (20.0)
Symptom status, n (%)							
Symptomatic	4 (36.4)	3 (27.3)	1 (9.1)	9 (25.7)	1 (100)	8 (38.1)	26 (28.9)

Table 2. Saliva: Numerical summary of evaluations *(Continued)*

Asymptomatic	3 (27.3)	0 (0)	1 (9.1)	0 (0)	0 (0)	2 (9.5)	6 (6.7)
Mixed	2 (18.2)	8 (72.7)	7 (63.6)	20 (57.1)	0 (0)	8 (38.1)	45 (50.0)
Unclear	2 (18.2)	0 (0)	2 (18.2)	6 (17.1)	0 (0)	3 (14.3)	13 (14.4)
Time of test, n (%)							
≤ 1 week post-symptom onset	2 (18.2)	2 (18.2)	3 (27.3)	7 (20.0)	1 (100)	5 (23.8)	20 (22.2)
≤ 2 weeks post-symptom onset	1 (9.1)	1 (9.1)	0 (0)	4 (11.4)	0 (0)	1 (4.8)	7 (7.8)
≤ 3 weeks post-symptom onset	1 (9.1)	0 (0)	0 (0)	2 (5.7)	0 (0)	0 (0)	3 (3.3)
≤ 3 weeks post-contact	0 (0)	0 (0)	0 (0)	1 (2.9)	0 (0)	0 (0)	1 (1.1)
Not stated	7 (63.6)	8 (72.7)	8 (72.7)	21 (60.0)	0 (0)	15 (71.4)	59 (65.6)
Sample collection (operator), n (%)							
Healthcare worker	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.8)	1 (1.11)
Self	7 (63.6)	6 (54.6)	5 (45.5)	24 (68.6)	1 (100)	15 (71.4)	58 (64.4)
Self-supervised	4 (36.4)	5 (45.5)	6 (54.6)	10 (28.6)	0 (0)	4 (19.1)	29 (32.2)
Not stated	0 (0)	0 (0)	0 (0)	1 (2.9)	0 (0)	1 (4.8)	2 (2.2)
Reference type, n (%)							
Nasopharyngeal	8 (72.7)	10 (90.9)	11 (100)	28 (80)	1 (100)	18 (85.7)	76 (84.4)
Combined nasopharyngeal/ oropharyngeal	3 (27.3)	1 (9.1)	0 (0)	7 (20.0)	0 (0)	3 (14.3)	14 (15.6)
Transport medium, n (%)							
Direct	6 (54.6)	5 (45.5)	6 (54.6)	12 (34.3)	0 (0)	13 (61.9)	42 (46.7)
Transport medium	4 (36.4)	6 (54.6)	3 (27.3)	17 (48.6)	0 (0)	5 (23.8)	35 (38.9)
Saline	0 (0)	0 (0)	0 (0)	1 (2.9)	0 (0)	0 (0)	1 (1.1)

Table 2. Saliva: Numerical summary of evaluations *(Continued)*

Water	0 (0)	0 (0)	1 (9.1)	0 (0)	0 (0)	0 (0)	1 (1.1)
Not stated	1 (9.1)	0 (0)	1 (9.1)	5 (14.3)	1 (100)	3 (14.3)	11 (12.2)
Same COVID-19 test kit, n (%)							
No	0 (0)	1 (9.1)	0 (0)	5 (14.3)	0 (0)	1 (4.8)	7 (7.8)
Yes	11 (100)	10 (90.9)	11 (100)	29 (82.9)	1 (100)	18 (85.7)	80 (88.9)
Not stated	0 (0)	0 (0)	0 (0)	1 (2.9)	0 (0)	2 (9.5)	3 (3.3)
COVID-19 test technology, n (%)							
Rapid antigen test	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Isothermal tests	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (9.5)	2 (2.2)
RT-PCR	11 (100)	10 (90.9)	11 (100)	34 (97.1)	1 (100)	19 (90.5)	86 (95.6)
Transcription-mediated amplification (TMA)	0 (0)	1 (9.1)	0 (0)	1 (2.9)	0 (0)	0 (0)	2 (2.2)

Abbreviations

COVID-19: coronavirus disease 19; IQR: interquartile range; n: number; RT-PCR: reverse transcription polymerase chain reaction; TMA: transcription-mediated amplification

Table 3. Nasal: Numerical summary of evaluations

	Anterior	Mid-turbinate	Not otherwise specified	Total
Number of test evaluations	15	19	3	37
Number of sample pairs (participants) [median (IQR)]	227 (104 to 932)	158 (90 to 290)	214 (182 to 369)	214 (104 to 369)
Number of COVID-19 cases [median (IQR)]	51 (14 to 78)	35 (16 to 51)	112 (12 to 112)	36 (16 to 73)
Setting, n (%)				
Community	2 (13.3)	3 (15.8)	0 (0)	5 (13.5)
Contact tracing	0 (0)	0 (0)	0 (0)	0 (0)
COVID-19 test centre	6 (40.0)	7 (36.8)	1 (33.3)	14 (37.8)
Inpatient	0 (0)	0 (0)	0 (0)	0 (0)
Mixed	2 (13.3)	1 (5.3)	0 (0)	3 (8.1)
Outpatient	5 (33.3)	6 (31.6)	1 (33.3)	12 (32.4)
Screening	0 (0)	0 (0)	0 (0)	0 (0)
Unclear	0 (0)	2 (10.5)	1 (33.3)	3 (8.1)
Age, n (%)				
Adult	11 (73.3)	12 (63.2)	1 (33.3)	24 (64.9)
Child	0 (0)	1 (5.3)	0 (0)	1 (2.7)
Mixed	4 (26.7)	2 (10.5)	1 (33.3)	7 (18.9)
Unclear	0 (0)	4 (21.1)	1 (33.3)	5 (13.5)
Symptom status, n (%)				
Symptomatic	4 (26.7)	7 (36.8)	3 (100)	14 (37.8)
Asymptomatic	1 (6.7)	0 (0)	0 (0)	1 (2.7)
Mixed	8 (53.3)	5 (26.3)	0 (0)	13 (35.1)
Unclear	2 (13.3)	7 (36.8)	0 (0)	9 (24.3)
Time of test, n (%)				
≤ 1 week post-symptom onset	5 (33.3)	5 (26.3)	3 (100)	13 (35.1)
≤ 2 weeks post-symptom onset	1 (6.7)	3 (15.8)	0 (0)	4 (10.8)

Table 3. Nasal: Numerical summary of evaluations *(Continued)*

≤ 3 weeks post-symptom onset	0 (0)	2 (10.5)	0 (0)	2 (5.4)
≤ 3 weeks post-contact	0 (0)	0 (0)	0 (0)	0 (0)
Not stated	9 (60.0)	9 (47.4)	0 (0)	18 (48.7)
Sample collection (operator), n (%)				
Healthcare worker (HCW)	5 (33.3)	5 (26.3)	1 (33.3)	11 (29.7)
Self	6 (40.0)	6 (31.6)	0 (0)	12 (32.4)
Self-supervised	2 (13.3)	4 (21.1)	0 (0)	6 (16.2)
Not stated	2 (13.3)	4 (21.1)	2 (66.7)	8 (21.6)
Reference type, n (%)				
Nasopharyngeal	15 (100)	18 (94.7)	3 (100)	36 (97.3)
Combined nasopharyngeal/oropharyngeal	0 (0)	1 (5.3)	0 (0)	1 (2.7)
Transport medium, n (%)				
Direct	3 (20.0)	3 (15.8)	1 (33.3)	7 (18.9)
Transport medium	12 (80.0)	12 (63.2)	1 (33.3)	25 (67.6)
Saline	0 (0)	0 (0)	0 (0)	0 (0)
Water	0 (0)	0 (0)	0 (0)	0 (0)
Not stated	0 (0)	4 (21.1)	1 (33.3)	5 (13.5)
Same COVID-19 test kit, n (%)				
No	0 (0)	3 (15.8)	0 (0)	3 (8.1)
Yes	15 (100)	14 (73.7)	3 (100)	32 (86.5)
Not stated	0 (0)	2 (10.5)	0 (0)	2 (5.4)
COVID-19 test technology, n (%)				
Rapid antigen test	3 (20.0)	4 (21.1)	1 (33.3)	8 (21.6)
Isothermal tests	1 (6.7)	1 (5.3)	0 (0)	2 (5.4)
RT-PCR	11 (73.3)	14 (73.7)	2 (66.7)	27 (73.0)
Transcription-mediated amplification (TMA)	0 (0)	0 (0)	0 (0)	0 (0)

Abbreviations

COVID-19: coronavirus disease 19; HCW: healthcare worker; IQR: interquartile range; n: number; RT-PCR: reverse transcription polymerase chain reaction; TMA: transcription-mediated amplification

Table 4. Other sample types (oropharyngeal; gargle; nasopharyngeal/oropharyngeal combined; operator; oral); numerical description of evaluations

	Oropharyn- geal	Gargle	Nasal/ oropharyn- geal (3 mid- turbinate, 1 anterior)	Operator (1 deep throat, 3 N/ A)	Oral	
					Oral rinse	Oral swab (1 buccal, 1 tongue, 2 not otherwise specified)
Number of test evaluations	7	6	4	4	2	4
Number of sample pairs (par- ticipants) [median (IQR)]	182 (146 to 353)	221.5 (23 to 645)	136.5 (71.5 to 279)	50 (47 to 133)	119 (98 to 140)	328.5 (121 to 500.5)
Number of COVID-19 cases [median (IQR)]	25 (12 to 105)	56.5 (9 to 129)	31 (20 to 49.5)	26 (24.5 to 34.5)	32.5 (30 to 35)	41.5 (29.5 to 99)
Setting, n (%)						
Community	0 (0)	0 (0)	0 (0)	1 (25.0)	1 (50.0)	0 (0)
Contact tracing	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
COVID-19 test centre	0 (0)	2 (33.3)	1 (25.0)	1 (25.0)	0 (0)	2 (50.0)
Inpatient	1 (14.3)	1 (16.7)	0 (0)	2 (50.0)	0 (0)	0 (0)
Mixed	2 (28.6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25.0)
Outpatient	2 (28.6)	0 (0)	3 (75.0)	0 (0)	0 (0)	1 (25.0)
Screening	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)
Unclear	2 (28.6)	2 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)
Age, n (%)						
Adult	4 (57.1)	4 (66.7)	4 (100)	4 (100)	1 (50.0)	1 (25.0)
Child	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mixed	1 (14.3)	1 (16.7)	0 (0)	0 (0)	1 (50.0)	1 (25.0)
Unclear	2 (28.6)	1 (16.7)	0 (0)	0 (0)	0 (0)	2 (50.0)
Symptom status, n (%)						
Symptomatic	4 (57.1)	1 (16.7)	2 (50.0)	2 (50.0)	0 (0)	2 (50.0)
Asymptomatic	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mixed	1 (14.3)	5 (83.3)	1 (25.0)	2 (50.0)	2 (100)	2 (50.0)

Table 4. Other sample types (oropharyngeal; gargle; nasopharyngeal/oropharyngeal combined; operator; oral); numerical description of evaluations *(Continued)*

Unclear	2 (28.6)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)
Time of test, n (%)						
≤ 1 week post-symptom onset	3 (42.9)	0 (0)	2 (50.0)	0 (0)	0 (0)	1 (25.0)
≤ 2 weeks post-symptom onset	1 (14.3)	0 (0)	1 (25.0)	0 (0)	0 (0)	1 (25.0)
≤ 3 weeks post-symptom onset	0 (0)	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)
≤ 3 weeks post-contact	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Not stated	3 (42.9)	6 (100)	1 (25.0)	3 (75.0)	2 (100)	2 (50.0)
Sample collection (operator), n (%)						
Healthcare worker (HCW)	4 (57.1)	0 (0)	2 (50.0)	1 (25.0)	0 (0)	0 (0)
Self	1 (14.3)	5 (83.3)	1 (25.0)	3 (75.0)	2 (100)	4 (100)
Self-supervised	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
Not stated	2 (28.6)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)
Reference type, n (%)						
Nasopharyngeal	5 (71.4)	4 (66.7)	3 (75.0)	2 (50.0)	2 (100)	4 (100)
Combined nasopharyngeal/ oropharyngeal	2 (28.6)	2 (33.3)	1 (25.0)	0 (0)	0 (0)	0 (0)
Transport medium, n (%)						
Direct	1 (14.3)	1 (16.7)	0 (0)	0 (0)	2 (100)	0 (0)
Transport medium	5 (71.4)	3 (50.0)	4 (100)	3 (75.0)	0 (0)	4 (100)
Saline	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
Water	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
Not stated	1 (14.3)	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)
Same COVID-19 test kit, n (%)						
No	1 (14.3)	0 (0)	0 (0)	0 (0)	0 (0)	2 (50.0)
Yes	6 (85.7)	4 (66.7)	4 (100)	4 (100)	2 (100)	2 (50.0)
Not stated	0 (0)	2 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)
COVID-19 test technology, n (%)						
Rapid antigen test	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Table 4. Other sample types (oropharyngeal; gargle; nasopharyngeal/oropharyngeal combined; operator; oral); numerical description of evaluations (Continued)

Isothermal tests	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
RT-PCR	7 (100)	6 (100)	4 (100)	4 (100)	2 (100)	4 (100)
Transcription-mediated amplification (TMA)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Abbreviations

COVID-19: coronavirus disease 19; HCW: healthcare worker; IQR: interquartile range; N/A: not applicable; n: number; RT-PCR: reverse transcription polymerase chain reaction; TMA: transcription-mediated amplification

Table 5. Study design and participant characteristics (a)

Study N (n SARS-CoV-2 cases)	Design and recruitment	Country, setting and dates	Participant characteristics	Missing data Uninterpretable/in-determinate results
			Exposure hospital	
			Timing of testing	
Abdollahi 2020a	Single group; adult patients with clinical and radiologic evidence of viral pneumonia admitted to an infectious diseases ward	Iran	AGE & SEX	MISSING DATA
Abdollahi 2020b		Inpatients	Median age 56 years (range 24 to 86); 32 (64%) male	None reported
50 (28)	Random, prospective	February 28 to April 27, 2020	SYMPTOMS	UNINTERPRETABLE
			Fever: 34 (68%) Muscle pain: 30 (60%) Cough: 30 (60%) Dyspnoea: 23 (46%) Chills: 8 (16%) Chest pain: 5 (10%) Loss of taste and/or smell: 4 (8%) Sneeze: 2 (4%) Abdo symptoms: 1 (2%)	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
AbdulRahman 2020	Unclear group of symptomatic individuals, staff, close contacts and pre-operation patients tested in a COVID-19 clinic	Bahrain	AGE & SEX	MISSING DATA
(AbdulRahman 2020a; AbdulRahman 2020b)		Hospital outpatient	Not stated	None reported
1009 (60)		October 2020	SYMPTOMS	UNINTERPRETABLE
			Not stated	None reported
			EXPOSURE	INDETERMINATE
			Not stated	None reported
Aita 2020	[1] Single group; 'Screening' participants enrolled from the community	Italy	AGE & SEX	MISSING DATA
326 (0)		Community	Not stated	None reported
			SYMPTOMS	UNINTERPRETABLE

Table 5. Study design and participant characteristics (a) *(Continued)*

	[2] 43 confirmed COVID-19 patients with saliva samples available tested during hospitalisation (not included) Recruitment unclear Prospective	April 22 to April 30, 2020	Not stated. Test application described as screening EXPOSURE HX Not stated	None reported INDETERMINATE None reported
Akgun Dogan 2021 (a) [1] 200 (98)	[1] Single group; Consecutive symptomatic patients who met the possible case definition for COVID-19 and hospitalised with moderate-severe disease, and sampled within the first 24 hours after hospitalisation (day 0) [2] Subgroup of patients re-tested on day 5 not included in analysis Consecutive, prospective	Turkey Inpatient Not stated	AGE & SEX Mean age 54.9 (SD ± 16.1); 160 (53%) male SYMPTOMS Cough: 120 (60%) Myalgia: 110 (55%) Fever: 80 (40%) Dyspnoea: 89 (45%) Loss of smell & taste: 13 (7%) EXPOSURE HX Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Al Suwaidi 2021 476 (80)	Single group of school children presenting for COVID-19 screening. Indications for testing included contact with confirmed COVID-19 patients, presence of presumptive symptoms or testing for return to school. Convenience sample Prospective	United Arab Emirates COVID-19 testing centre 1 to 23 October, 2020	AGE & SEX Age: Mean (SD): 10.8 (3.9) Sex: 277/476 (58.2%) male SYMPTOMS 39/476 (8.1%) symptomatic EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Altawalah 2020 891 (362)	Single group of suspected COVID-19 patients admitted consecutively to the Al-Sabah, Jaber, and Alrazi Hospitals, Kuwait Consecutive Prospective	Kuwait Hospital inpatient 19 to 21 July, 2020	AGE & SEX Age: Not stated Sex: Not stated for whole sample. For NP +ve 193/344 (56.1%) male SYMPTOMS Not stated EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE 43 NP and 28 saliva samples equivocal. No 3 x 3 data provided
Amoo 2021 216 (42)	Asymptomatic and symptomatic individuals > 15 yrs presenting for testing at a drive-through COVID-19 centre Recruitment unclear: Individuals who gave verbal consent were enrolled	Nigeria COVID-19 testing centre/drive-through	AGE & SEX Age: Mean 35 (SD ± 14.2) Sex: 122/216 (56.5%) male	MISSING DATA None reported UNINTERPRETABLE

Table 5. Study design and participant characteristics (a) *(Continued)*

	Prospective	June-July 2020	SYMPTOMS 113/216 (52.3%) symptomatic EXPOSURE 128/216 (59.3%) with known exposure to COVID-19 case 12/216 (5.6%) had contact with overseas travellers	None reported INDETERMINATE None reported
Babady 2021 [A&B] [1] 98 (35) [2] 87 (18)	[1] Single group of MSKCC employees who completed an internally designed research electronic data capture screening tool designed to determine the need for COVID-19 testing, and with paired oral rinses and NP samples [2] Single group of MSKCC employees who completed an internally designed research electronic data capture screening tool designed to determine the need for COVID-19 testing, and with paired saliva and NP samples [3] Single group of MSKCC employees who completed an internally designed research electronic data capture screening tool designed to determine the need for COVID-19 testing, and with paired saliva and OP samples. Not extracted for this review (ineligible reference index sample) Recruitment unclear Prospective	USA Other: HCW screening April 4 to May 11, 2020	AGE & SEX Not stated SYMPTOMS 224/285 (78.5%) symptomatic EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Banerjee 2021 110 (59) Note this is an artificial prevalence as base on matching cases and non-cases to achieve a prevalence of ~50%	Single group of 335 children who had standard of care COVID-19 testing ordered by their health care provider Recruitment unclear Prospective	USA COVID-19 testing centre Not stated	AGE & SEX Age: Mean (range): 10.8 years (5-14) Sex: 55/110 (50.5%) males SYMPTOMS 100/109 (91.7%) symptomatic EXPOSURE 9/110 (8.1%) were asymptomatic with known COVID-19 exposure	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Becker 2020 [1] 88 (17)	[1] Single group; Symptomatic patients who met CDC criteria for clinical testing	USA Community March 26 to April 12, 2020	AGE & SEX Not stated SYMPTOMS	MISSING DATA [1] 17 saliva samples were not evaluated

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Table 5. Study design and participant characteristics (a) *(Continued)*

	[2] Single 'Convalescent cohort' prior positive NPS hospitalised at time of first testing. Not included in analysis		Symptomatic meeting CDC criteria for clinical testing	(UCSD) and 6 NP samples 'not ordered' by the attending physician
	Recruitment unclear		EXPOSURE HX	
	Prospective		Not stated	UNINTERPRETABLE
				None reported
				INDETERMINATE
				[1] 6 indeterminate UCSD TaqPath NP; 3 indeterminate UCSD TaqPath saliva; 2 indeterminate Helix Primerdesign v1 saliva
Begum 2022	A cross-sectional study. Inclusion criteria were (i) all age groups (ii) either sex; (iii) acute onset of fever or cough; OR (iv) acute onset of any three or more of the presented signs or symptoms, general weakness/fatigue, headache, myalgia, sore throat, runny nose, nasal congestion, dyspnoea, anorexia/ nausea/vomiting, diarrhoea, and altered mental status.	Bangladesh	AGE & SEX	MISSING DATA
214 (112)		Unclear	Age: Not stated Sex: Not stated	None reported
		May and August 2021	SYMPTOMS	UNINTERPRETABLE
			214/214 (100%) symptomatic	None reported
			EXPOSURE	INDETERMINATE
	Unclear recruitment: 214 symptomatic participants who fulfilled WHO case definitions for COVID-19 and who had known rRT-PCR test results within the last 24 h, using NP swab.		Not stated	None reported
	Retrospective			
Benoit 2021	Single group of participants recruited from a dedicated COVID-19 screening clinic to see if they had symptoms of COVID-19 or if they had contact with a positive case	Canada	AGE & SEX	MISSING DATA
647 (134)		COVID-19 testing centre	Not stated	None reported
	Consecutive	November and December 2020	SYMPTOMS	UNINTERPRETABLE
	Prospective		Not stated Quote: "Participants were recruited if they had symptoms of COVID-19 or if they had contact with a positive case"	3 participants with invalid results (excluded before processing) excluded for main analysis
			EXPOSURE	INDETERMINATE
			Not stated	None reported
Bhattacharya 2021	Single group; suspected COVID-19 patients with mild-to-moderate symptoms from different COVID-19 care hospitals in Bhubaneswar, India	India	AGE & SEX	MISSING DATA
74 (58)		Unclear	Not stated	None reported
		Not stated	SYMPTOMS	UNINTERPRETABLE
	Recruitment: Not stated Prospective			None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

			Mild-to-moderate symptoms	INDETERMINATE
			EXPOSURE HX	None reported
			Not stated	
Bidkar 2022	Single group of suspects aged 8 years and above presenting with a varied spectrum of illness of COVID-19	India	AGE & SEX	MISSING DATA
80 (40)	Consecutive	Hospital outpatient	Mean age: 36.4 yrs 49/80 (61.3%) males	None reported
	Prospective	October-November 2020	SYMPTOMS	UNINTERPRETABLE
			Not stated	None reported
			EXPOSURE	INDETERMINATE
			Not stated	Inconclusive samples: 4 NP and 6 salivary samples
Bikos 2021	Unclear group of individuals testing at the Montana State University (MSU) symptomatic testing site in Bozeman, MT, USA between the days of mid-November 2020	USA	AGE & SEX	MISSING DATA
243 (70)	Recruitment unclear (probably volunteers)	COVID-19 testing centre	Age: median (range): 20 (17-63) Sex: 112/244 (45%) male	None reported
	Prospective	Mid-November 2020	SYMPTOMS	UNINTERPRETABLE
			170/243 (70%) symptomatic	None reported
			EXPOSURE	INDETERMINATE
			Not stated	None reported
Boerger 2021 (A&B)	Single group of adults, aged 18 or older, who presented at an outpatient collection site for SARS-CoV-2 molecular testing	USA	AGE & SEX	MISSING DATA
281 (35)	Recruitment unclear	Hospital outpatient	Not stated	51 samples not included in final paired analysis
	Prospective	Not stated	SYMPTOMS	UNINTERPRETABLE
			Not stated	None reported
			EXPOSURE	INDETERMINATE
			Not stated	1 (0.3%) NP swab and 4 (1.4%) saliva specimens yielded an indeterminate result.
Borghi 2021 (Borghi 2021a; Borghi 2021b)	Single group of adults with paired samples attending the San Paolo Hospital in Milan	Italy	AGE & SEX	MISSING DATA
192 (87)	Recruitment unclear	Hospital, no further details provided	Age: range 18–85 years Sex: 91/192 (47.8%) males	None reported
	Prospective	Not stated	SYMPTOMS	UNINTERPRETABLE
			80/192 (41.7%)	None reported
			EXPOSURE	INDETERMINATE

Table 5. Study design and participant characteristics (a) *(Continued)*

			Not stated	None reported
Borghi 2021c 109 (27)	Single group of children with paired samples attending at Vittore Buzzi Children Hospital Recruitment unclear Prospective	Italy Hospital, no further details provided Not stated	AGE & SEX Age from 0-17 years Sex: 58/109 (53.6%) males SYMPTOMS [a] 80/192 (41.7%) [b] Not stated EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Boutros 2021(a) 147 (59)	Adults referred by their attending physician because of recent symptoms of COVID-19 Consecutive Prospective	France COVID-19 testing centre/drive-through 21 September 2020-6 January, 2021	AGE & SEX Mean age 40 (SD 15) Sex: 61/147 (41.4%) male SYMPTOMS 147/147 (100%) EXPOSURE Not stated	MISSING DATA Some patients declined to perform NP once OP had been performed (n = 2) UNINTERPRETABLE None reported INDETERMINATE None reported
Boutros 2021 (b) 262 (57)	Adults referred by the contact tracing staff of the French public health insurance, considered as close contacts of a laboratory-confirmed COVID-19 case Consecutive Prospective	France COVID-19 testing centre/drive-through 6 February-8 March, 2021	AGE & SEX Mean age 41 (SD 15) Sex: 117/262 (44.6%) male SYMPTOMS 0/262 (0%) EXPOSURE [b] 262/262 (100%) with known exposure to COVID-19 case	MISSING DATA Some patients declined to perform NP once OP had been performed (n = 2) UNINTERPRETABLE None reported INDETERMINATE None reported
Bruxvoort 2021 [A&B] 2112 (335)	Single group of adult patients presenting to EDs with acute symptoms concerning for COVID-19 were eligible to participate in the study if their attending physician placed an order for a standard NP/OP SARS-CoV-2 test. Only patients with all three specimens collected were included in main analysis. Prospective	USA Emergency Department 18 August to 2 November, 2020	AGE & SEX Age: 864/2112 (40.9%) 18-39 years 647/2112 (30.6%) 40-59 years 601/2112 (28.5%) ≥ 60 years Sex: 952/2112 (45.1%) male SYMPTOMS All participants symptomatic at testing time	MISSING DATA 81 pairs excluded due to one of the samples being missing UNINTERPRETABLE None reported INDETERMINATE None reported

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Table 5. Study design and participant characteristics (a) *(Continued)*

			EXPOSURE	
			Not stated	
Callahan 2021a-d (Callahan 2021(a); Callahan 2021(b); Callahan 2021(c); Callahan 2021(d))	[1] Single group of participants presenting for their first COVID-19 test "clinically suspected of COVID-19"	USA	AGE & SEX	MISSING DATA
		Unclear	Not stated	None reported
	[2] single group of participants with a previous positive test presenting for follow-up [preselected population, not extracted]	Not stated	SYMPTOMS	UNINTERPRETABLE
			Not stated "Clinically suspected of COVID-19"	None reported
[1] Initial (general): 196 (35) This was calculated by adding up TP, FN and FP for shallow and deep nasal samples combined in the initial tested group	Recruitment unclear		EXPOSURE	INDETERMINATE
	Unclear prospective/retrospective		Not stated	None reported
Callahan 2021(e) Initial assessment: 343 (68)	Unclear group of adults presenting for either initial or follow-up testing for COVID-19. Only initial testing group data extracted for this review. Participants included a mix of symptomatic and asymptomatic patients.	USA	AGE & SEX	MISSING DATA
		COVID-19 testing centre	Not stated	None reported
		Not stated	SYMPTOMS	UNINTERPRETABLE
			Mix of symptomatic and asymptomatic; no details provided	None reported
	Convenience: "After several days of collection, resulting in a majority of negatives, only (NP) positives were included to minimise clinical burden on laboratory staff".		EXPOSURE	INDETERMINATE
	Prospective		Not stated	Leaking samples and internal-control failures were omitted from analysis.
Castelain 2021 501 (26)	Single group of 501 individuals from residential care homes for the elderly (193 residents, 308 caregivers and administrative staff) participated in screening for SARS-CoV-2.	France	AGE & SEX	MISSING DATA
		Other (residential care homes)	Age mean (SD): 56.3 ± 22,2 102/501 (20.4%) males	None reported
	Recruitment unclear	6 to 13 May, 2020	SYMPTOMS	UNINTERPRETABLE
			104/501 (20.7%) symptomatic	None reported
	Prospective		EXPOSURE	INDETERMINATE
			Not stated	None reported
Chu 2021 (a) [A&B] 300 (33)	Single group of eligible ambulatory participants who presented to Groote Schuur Hospital in Cape Town, South Africa, for SARS-CoV-2 testing, before replacement of wild-type virus with the beta VoC	South Africa	AGE & SEX	MISSING DATA
		Hospital outpatient	Not stated	None reported
		1 August 2020 to 16 January, 2021	SYMPTOMS	UNINTERPRETABLE
			Not stated	None reported
	Recruitment unclear		EXPOSURE	INDETERMINATE

Table 5. Study design and participant characteristics (a) *(Continued)*

	Prospective		Not stated	None reported
Chu 2021 (b) [A&B] 107 (40)	Single group of eligible ambulatory participants who presented to Groote Schuur Hospital in Cape Town, South Africa, for SARS-CoV-2 testing, after replacement of wild-type virus with the beta VoC Recruitment unclear Prospective	South Africa Hospital outpatient 1 August 2020 to 16 January, 2021	AGE & SEX Not stated SYMPTOMS Not stated EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Congrave-Wilson 2021 889 (584)	Single group of symptomatic and asymptomatic individuals exposed to a household member with RT-PCR-confirmed SARS-CoV-2 within 2 weeks "Convenience sample", contact tracing investigation? Unclear prospective/retrospective	USA Mixed: Hospital and community testing centres 17 June 2020 to 15 February, 2021	AGE & SEX Mean age (range): 28.2 (3.0-84.5) 108/404 (42.2%) male SYMPTOMS 93/404 (36.3%) asymptomatic 126/404 (31.1%) reported mild severity EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Cradic 2020 182 (12)	Single group; Symptomatic patients suspected of COVID-19 meeting criteria for testing. NP swab collection intended for routine testing; OP and nasal samples collected from patients who consented to subsequent additional sample collection. Described as a quality improvement study. NP swab collection part of routine testing for patients presenting with signs and/or symptoms of COVID-19 infection. OP and nasal samples collected from patients who consented to subsequent additional sample collection Prospective	USA Emergency Department Not stated	AGE & SEX Not stated SYMPTOMS All symptomatic EXPOSURE HX Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Da Silva 2022 61(19)	Single group study Samples collected from symptomatic patients and asymptomatic patients who were in contact with either positive or suspected cases Recruitment unclear Prospective	Brazil COVID-19 testing centre/drive-through August-September, 2020	AGE & SEX Not stated SYMPTOMS Not stated EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
De Oliveira 2021 400 (157)	Single group of adults (n = 403) seeking routine RT-PCR for SARS-CoV-2	Brazil Unclear	AGE & SEX Not stated	MISSING DATA None reported

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Table 5. Study design and participant characteristics (a) *(Continued)*

	Recruitment unclear	October to November, 2020	SYMPTOMS	UNINTERPRETABLE
	Prospective		325/400 (81.2%) symptomatic	None reported
			EXPOSURE	INDETERMINATE
			Not stated	3 paired samples excluded due to saliva samples showing an invalid result
Desai 2021(a) [A-C] (Desai 2021(a) [A]; Desai 2021(a) [B]; Desai 2021(a) [C])	Single group of 128 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing at the Wisconsin site	USA	AGE & SEX	MISSING DATA
	Single group of 55 symptomatic COVID-19-confirmed positive patients admitted for observation and management at the New Jersey site (not extracted for this review)	COVID-19 testing centre	[a] No information provided	None reported
From extracted 2 x 2 tables taking the sample pairs with the most D+ on either sample pair: 117 (16)	Recruitment unclear	December 2020 to April, 2021	SYMPTOMS	UNINTERPRETABLE
	Prospective		No information provided	None reported
			EXPOSURE	INDETERMINATE
			Not stated	1.0% of NP, 1.4% of anterior nares, 3.9% of mid-turbinate, and 0% of saliva samples had invalid results.
Desai 2021(b)	Single group of 900 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing at the Salvador site and single group of 265 asymptomatic and symptomatic subjects presenting for SARS-CoV-2 testing at the Paraguay site (analysed together)	El Salvador and Paraguay	AGE & SEX	MISSING DATA
From extracted 2 x 2 tables taking the sample pairs with the most D+ on either sample pair: 1153 (230)	Single group of 55 symptomatic COVID-19-confirmed positive patients admitted for observation and management at the New Jersey site (not extracted for this review)	COVID-19 testing centre	[El Salvador]	None reported
	Recruitment unclear	December 2020 to April, 2021	Age:	UNINTERPRETABLE
	Prospective		18-28 yrs: 204/900 (22.7%);	None reported
			29-39 yrs: 242/900 (26.9%);	INDETERMINATE
			40-50 yrs: 222/900 (24.7%);	1.0% of NP, 1.4% of anterior nares, 3.9% of mid-turbinate, and 0% of saliva samples had invalid results.
			≥ 50 yrs: 232/900 (25.8%)	
			Sex: 425/900 (47.2%) male	
			[Paraguay]	
			Age	
			18-28 yrs: 118/265 (44.5%);	
			29-39 yrs: 74/265 (27.9%);	
			40-50 yrs: 41/2650 (15.5%);	
			≥ 50 yrs: 32/265 (21.1%)	
			Sex: 106/265 (40%) male	
			SYMPTOMS	
			[El Salvador] 272/900 (30.2%) symptomatic	
			[Paraguay] 207/265 (78.1%) symptomatic	
			[a] No information provided	

Table 5. Study design and participant characteristics (a) *(Continued)*

			EXPOSURE	
			Not stated	
Desmet 2020	[1] Single group; Patients presenting to the Emergency Department suspected of COVID-19, based on respiratory and inflammatory symptoms [2] Single group; Subgroup of patients from [1] admitted to hospital with highly-suspect clinical and radiological features of COVID-19 not extracted for this review Consecutive, prospective	Belgium Emergency Department 7 April to 1 May, 2020	AGE & SEX Median age 61 years (range 22-90); 21 (58%) male SYMPTOMS All symptomatic with respiratory and inflammatory symptoms; 28 (78%) required hospitalisation EXPOSURE HX Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Dumaresq 2021	Single group of asymptomatic and symptomatic individuals aged ≥ 6 years presenting to a drive-through test centre Recruitment unclear Prospective	Canada COVID-19 drive-through centre 8 to 23 October, 2020	AGE & SEX Age: Median (range): 40 (6-91) Sex: NS SYMPTOMS 633/1005 (63%) were symptomatic EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE Results were invalid for 2.7% (27 of 1005) ONPS and for 0.9% (9 of 1005) gargles; results retested by a second RT-PCR (unclear if reflected in the first 2 x 2 table/ Figure 1)
Echavarria 2021	Single group of symptomatic patients presenting at the emergency room (ER) in CEMIC University Hospital from August to September 2020 Recruitment unclear Prospective	Argentina Emergency Department August to September, 2020	AGE & SEX Median age (IQR): 38 (31-50) 70/174 (40.2%) male SYMPTOMS All patients symptomatic at testing 9/174 (5.2%) required hospitalisation. 1/174 (0.5%) was admitted to the ICU. Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Escobar 2021	Samples were collected from symptomatic and asymptomatic individuals and from people who were in close con-	Chile	AGE & SEX Age: range 11-77	MISSING DATA 2 ineligible (NOS)

Table 5. Study design and participant characteristics (a) *(Continued)*

	tact with COVID-19 confirmed cases or who were clinically suspicious presenting to hospital (ambulatory) or the community.	Mixed hospital (probably OP) and community	Sex: 68/127 (53.3%) male	UNINTERPRETABLE
	Recruitment unclear	February 2021	SYMPTOMS 111/127 (87.4%) symptomatic	Excluded samples (n = 2) due to lack of amplification internal control to reference methodology and lack of amplification internal control to candidate methodology
	Prospective		EXPOSURE 21/127 (16.5%) with known exposure to COVID-19 case	INDETERMINATE None reported
Felix 2022	Single group Symptomatic children with suspected COVID-19	Brazil	AGE & SEX	MISSING DATA
50 (10)		Unclear	Median age: 10.24 ± 3.52	None reported
	Recruitment unclear	Unclear	Sex: 23/50 (46%) male	UNINTERPRETABLE
	Prospective		SYMPTOMS 46/50 (92%) symptomatic at time of testing	None reported
			EXPOSURE Not stated	INDETERMINATE None reported
Da Costa Fernandes 2021	Single-group study Patients oriented to perform the detection of SARS-CoV-2 because of either having experienced high-risk contacts with positive COVID-19 patients or because of showing symptoms potentially indicative of COVID-19.	Portugal	AGE & SEX	MISSING DATA
(a) 226 (84) (no RNA extraction) (b) 92 (76) (RNA extraction)	Recruitment unclear: (452 samples were collected for the present work between 14 December 2020 and 27th January, 2021)	Unclear	Age: NS Sex: 99/26 (39%) male	None reported
		14 December 2020 to 27 January, 2021	SYMPTOMS Not stated	UNINTERPRETABLE None reported
			EXPOSURE Not stated	INDETERMINATE None reported
	Unclear, probably prospective			
Fernandez-Gonzalez 2021(a); Fernandez-Gonzalez 2021(b); Fernandez-Gonzalez 2021 (c)	Single group study of asymptomatic and symptomatic patients presenting for SARS-CoV-2 testing, as requested by their providers, at the facilities of three primary care centres	Spain	AGE & SEX	MISSING DATA
[A 229 (50)- saliva supervised collection [B] 140 (27)- oropharyngeal washing [C] 208 (42)- saliva self collection	Consecutive Prospective	Community (primary care centre) 15 September to 29 October, 2020	Age: median (range): 39 (24-51) Sex: 251/577 (43.5%) male SYMPTOMS 336/577 (58.2%) symptomatic EXPOSURE Not stated	Fifty-four patients (median [Q1 to Q3] age, 5.8 [4 to 10] years; 44 children) were unable to provide saliva specimens, and 3 (0.5%) specimens had insufficient samples for laboratory analysis. UNINTERPRETABLE None reported INDETERMINATE

Table 5. Study design and participant characteristics (a) *(Continued)*

				Reported in table 2 in the paper
Fernández-Pittol 2020	Single group; patients presenting to ED with laboratory or clinical-radiologic findings compatible with a diagnosis of COVID-19: 'clinically diagnosed as having COVID-19'.	Spain	AGE & SEX	MISSING DATA
51 (37)	Consecutive	Emergency department	Not stated	None reported
	Prospective	Not stated	SYMPTOMS	UNINTERPRETABLE
			Laboratory or clinical-radiologic findings compatible with a diagnosis of COVID-19. 28/51 (14%) < 9 days since the onset of symptoms	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
FIND (a) 2021	Single group adults in community meeting national COVID-19 suspect definition. No further details	Brazil	AGE & SEX	MISSING DATA
218 (79)	Consecutive	COVID-19 testing centre/drive-through	Age: mean (range) 42.3 (18-90)	None reported
	Prospective	21 to 27 January, 2021 and 23 to 26 February, 2021	Sex: 92/218 (42%) male	UNINTERPRETABLE
			SYMPTOMS	None reported
			218/218 (100%) symptomatic	INDETERMINATE
			EXPOSURE	None reported
			Not stated	
FIND (b) 2021	Single group of adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting suspect definition of the Department of Public Health. No further details	Germany	AGE & SEX	MISSING DATA
281 (22)	Consecutive	COVID-19 testing centre/drive-through	Age: mean (range): 42.9 (18-81)	None reported
	Prospective	15 December 2020 to 19 January, 2021	Sex: 134/280 (47.9%) male	UNINTERPRETABLE
			SYMPTOMS	None reported
			Symptoms: 130/279 (46.2%)	INDETERMINATE
			EXPOSURE	None reported
			Not stated	
FIND (c) 2021(a)	Adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting suspect definition of the Department of Public Health	Berlin	AGE & SEX	MISSING DATA
179 (42)	Consecutive	COVID-19 testing centre/drive-through	Age: mean (range) 36.2 (18-72)	None reported
	Prospective	11-18 November 2020	Sex: 93/179 (52%)	UNINTERPRETABLE
			SYMPTOMS	None reported
			173/179 (96.6%)	INDETERMINATE
			EXPOSURE	None reported
			Not stated	

Table 5. Study design and participant characteristics (a) *(Continued)*

FIND(c) 2021 (b) 214 (78)	Single group of adults in the community meeting national suspect definition for COVID-19 nos Consecutive Prospective	Brazil COVID-19 test- ing centre/dri- ve-through 14-20 January, 2021; 2-4 March, 2021	AGE & SEX Age: mean (range) 41.31 (18-77) Sex: 85/214 (40%) SYMPTOMS 214/214 (100%) EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
FIND(s) 2021 369 (121) (NPS RT-PCR reference standard)	Single group of symptomatic adults pre- senting to a dedicated COVID-19 dri- ve-through testing centre to determine the accuracy of COVID-19 antigen RDTs, using consecutive enrolment Consecutive Prospective	UK COVID-19 test- ing centre/dri- ve-through 16 September-14 October, 2021	AGE & SEX Age: mean (range) 43 (18-831) Sex: 159/369 (43%) male SYMPTOMS Symptomatic: 369/369 (100%) EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE 6 invalid nasal Ag (in- dex)samples 1 invalid NPS Ag in- dex reference sam- ples INDETERMINATE None reported
Fougere 2021 397(106)	Single group of children presenting with symptoms compatible with COVID-19 according to 'national guidelines' Unclear (children 1 month to 18 years of age were recruited from 2 different out- patient clinics in Lausanne). Children > 12 years had to report at least one major symptom (fever, respiratory symptoms such as cough, throat pain, dyspnoea or thoracic pain, anosmia, dysgeusia) or 1 minor symptom + contact with a con- firmed COVID-19 case. Testing criteria were 'more strict' for children < 12 years (no further details). Prospective	France Hospital outpa- tient Unclear	AGE & SEX Age: mean 12.7 ± 3.8 Sex: 205/397 (52%) male SYMPTOMS All (100%) symptomatic EXPOSURE Not stated	MISSING DATA 878 tested at setting, of which 405 includ- ed in this study. Re- sults available for 397. No further de- tails were provided. At least 8 sample pairs missing data UNINTERPRETABLE Not stated INDETERMINATE Not stated
Fronza 2021 (a) 32 (15)	Single group of individuals undergo- ing testing for having recently been in contact with infected persons (contact tracing), convalescent individuals test- ed to confirm their recovery, healthcare professionals for routine screening or symptomatic individuals suspected of infection Symptomatic n = 32 422 asymptomatic convalescent and 336 asymptomatic screened HCW could not be disaggregated and so not includ- ed in this review.	Italy COVID-19 test- ing centre/dri- ve-through 25 March to 23 April, 2021	AGE & SEX Age: mean 41.7 (SD 15.2) Sex: 434/1003 (43%) male (included prior tested individuals not included in this review and the population from Fron- za) (b) SYMPTOMS	MISSING DATA 22/1025 (2%) tubes containing visibly less than 0.5 mL of oral fluid (saliva) were excluded UNINTERPRETABLE None reported INDETERMINATE None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

	Recruitment unclear			32/32 (100%) symptomatic
	Prospective			EXPOSURE
				193/1003 (19%) with known exposure to COVID-19 case 442/1003 (44%) previous COVID-19 infection (included prior tested individuals not included in this review and population from Fronza)
				(b)
Fronza 2021 (b)	Single group of individuals undergoing testing for having recently been in contact with infected persons (contact tracing), convalescent individuals tested to confirm their recovery, healthcare professionals for routine screening or symptomatic individuals suspected of infection [b] Asymptomatic contact tracing, n = 193 422 asymptomatic convalescent and 336 asymptomatic screened HCW could not be disaggregated and so not included in this review Unclear recruitment Prospective	Italy COVID-19 testing centre/drive-through 25 March to 23 April, 2021	AGE & SEX Age: mean 41.7 (SD 15.2) Sex: 434/1003 (43%) male (included prior tested individuals not included in this review and population from Fronza) (a) SYMPTOMS 0/193 (0%) symptomatic EXPOSURE 193/1003 (19%) with known exposure to COVID-19 case 442/1003 (44%) previous COVID-19 infection (included prior tested individuals not included in this review and population from Fronza) (a)	MISSING DATA 22/1025 (2%) tubes containing visibly less than 0.5 mL of oral fluid (saliva) were excluded. UNINTERPRETABLE None reported INDETERMINATE None reported
Goncalves 2021 [A&B]	Unclear group of mild-symptomatic and asymptomatic subjects tested in Rio de Janeiro state Recruitment unclear Unclear prospective/retrospective	Brazil Mixed hospital outpatient and COVID-19 testing centre Not stated	AGE & SEX [A] Age: mean (SD): 39 ± 13 yrs Sex: 150/158 (31.6%) males [B] Age: mean (SD): 43 ± 15.5 yrs Sex: 109/207 (52.6%) male SYMPTOMS [A] 6/158 (3.82%) asymptomatic	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE 1 indeterminate and 3 inconclusive nasopharyngeal samples

Table 5. Study design and participant characteristics (a) *(Continued)*

				Mean days from the onset of symptoms to sample collection: 4.71 $\pm$ 2.37 [B] 38/207 (18.36%) asymptomatic Mean days from the onset of symptoms to sample collection: 7.11 $\pm$ 11.39 EXPOSURE Not stated
Griesemer 2021 (a) [A&B] 236 (12)	Single group of patients for COVID-19 testing; without an appointment and also without the requirement of being symptomatic from Albany Medical Center (AMC) Emergency Department parking lot (n = 236) Recruitment unclear (collected between 20 and 26 March, 2020) Prospective	USA Emergency department Between 20 and 26 March, 2020	AGE & SEX Age: range 3-105 Sex: 111/236 (47%) male SYMPTOMS Not stated EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Griesemer 2021 (b) [A&B] 227 (93)	Single group of patients for COVID-19 testing; with the requirement of having an appointment and qualifying symptoms or exposures, from drive-through Regional Operations Centre (ROC) in New Rochelle (n = 227) Recruitment unclear (collected between 20 and 26 March, 2020) Prospective	USA COVID-19 test centre/drive-through Between 20 and 26 March, 2020	AGE & SEX Age: range 14-77 Sex: 136/227 (60%) male SYMPTOMS Not stated EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Guclu 2020 (a) 15 (5)	Single group study; inpatients admitted from A&E (day 0) with normal CT but signs and symptoms compatible with COVID-19 (15) [See Guclu 2020 (b) for report of two-group study of symptomatic patients with (30) and without (19) PCR-confirmed COVID-19 infection] Recruitment unclear Prospective	Turkey Emergency department Not stated	AGE & SEX For Guclu 2020 (a) and Guclu 2020 (b) combined: Mean age 51 (SD $\pm$ 17.9); 37 (57.8%) male SYMPTOMS Symptomatic (fever, cough, shortness of breath) but normal CT findings after examination by the 'head doctor' EXPOSURE HX Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Guclu 2020 (b)	Two group study; inpatients (day 3) with symptoms and CT findings compatible	Turkey	AGE & SEX	MISSING DATA

Table 5. Study design and participant characteristics (a) *(Continued)*

49 (30)	with COVID-19 with [30] and without [19] PCR confirmed COVID-19 infection	Inpatient Not stated	For Guclu 2020 (a) and Guclu 2020 (b) combined: Mean age 51 (SD ± 17.9); 37 (57.8%) male	None reported UNINTERPRETABLE
	[See Guclu 2020 (a) for report of single-group study of 15 symptomatic patients] Recruitment: not stated Prospective		SYMPTOMS Symptomatic (fever, cough, shortness of breath) and CT findings compatible with COVID-19 after examination by the 'head doctor' EXPOSURE HX Not stated	None reported INDETERMINATE None reported
Guzman-Ortiz 2021	[1] single group of paediatric participants who were COVID-19 non-confirmed or non-suspected patients [2] single group of paediatric participants confirmed positive for SARS-CoV-2 who were recovering at a COVID-19-specific area (preselected population of D+, not extracted for this review) [3] single group of adult participants, members of the hospital staff from all departments (selective testing of NP/OP negatives, not extracted for this review) Unclear: "...the clinical criterion was the presence of at least one symptom related to SARS-CoV-2 infection. The exclusion criteria were: declined to participate and not provided enough of a saliva sample." In figure 1, 73 exclusions were because "no saliva sample was collected". Prospective	Mexico Hospital inpatient/outpatient 4 May to 28 August, 2020	AGE & SEX Age: median (IQR): 11 years (7-14) Sex: 78/156 (50%) male SYMPTOMS 91/156 (58.3%) symptomatic 128/156 ~ (82%) concurrent medical condition EXPOSURE Not stated	MISSING DATA 26 saliva specimens not tested: 6 saliva specimens not tested because of inadequate storage (5 days at 40 °C) and 20 samples with inadequate volume UNINTERPRETABLE None reported INDETERMINATE Test in saliva inconclusive '0'
Hamilton 2021	Unclear group of paired nasopharyngeal (NP) swab and saliva specimens from symptomatic individuals during the months of August and September of 2020 Unclear recruitment Retrospective	USA Hospital outpatients August to September, 2020	AGE & SEX Not stated SYMPTOMS All participants were symptomatic at testing time. EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE 1 invalid data for the IGI NP assay, 5 for the IGI saliva assay INDETERMINATE None reported
Herrera 2021	Single group of consecutive asymptomatic healthcare and office workers Consecutive Prospective	Mexico Community Not stated	AGE & SEX Not stated SYMPTOMS	MISSING DATA None reported UNINTERPRETABLE None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

			All participants asymptomatic at enrolment	INDETERMINATE
			EXPOSURE	40 for NP swabs, 20 for saliva samples
			Not stated	
Huber 2021 (a); Huber 2021 (b); Huber 2021 (c)	Single group asymptomatic and symptomatic adults and children opting for a voluntary SARS-CoV-2 test with SARS-CoV-2-related symptoms based on Swiss testing criteria and asymptomatic individuals with relevant exposure to a SARS-CoV-2 index case at one of four dedicated outpatient testing centres or 1 AE department. Could be subgrouped into [1] mixed [2] adults and [3] children Consecutive: "Individuals were included without further selection to avoid skewing". Prospective	Switzerland Dedicated outpatient test centres and emergency department From 20 October 2020 to 28 January, 2021	AGE & SEX Age: median 34 (IQR 5-98) sex: 693/1270 (54.6%) male SYMPTOMS 960/1270 (75.6%) symptomatic EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Justo 2021	Single group of São Paulo hospital workers presenting with mild symptoms such as cough, fever, sore throat, rhinorrhoea, myalgia, headaches, insomnia, ageusia and fatigue. Recruitment unclear Prospective	Brazil Other (HCW undergoing screening at their place of work) October to December, 2020	AGE & SEX Mean age (range): 34.9 years (19-70) Sex: 23/76 (30.2%) male SYMPTOMS 76/76 (100%) symptomatic EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Kannian 2021	Single group of patients with suspected COVID-19 symptoms recruited from the outpatient department and COVID-19 isolation wards Recruitment unclear Retrospective	India Hospital (outpatient and inpatient) Not stated	AGE & SEX Information from COVID-19+ only on Table 3: 34/55 (62%) male 17/55 (31%) between 20-40 years 21/55 (38%) between 41-60 years 17/55 (31%) ≥ 61 years SYMPTOMS All patients symptomatic at testing Information from COVID-19+ only in Table 3: 16/55 (29%) mild disease 33/55 (60%) moderate disease 6/55 (11%) severe disease	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

			EXPOSURE	
			Not stated	
Kerneis 2021 (a) ; Kerneis 2021 (b) ; Kerneis 2021 (c) 1328 (112):	Single group of adults and children, either symptomatic or asymptomatic, referred to the two participating ambulatory community screening COVISAN centres in France	France	AGE & SEX	MISSING DATA
	Consecutive Prospective	COVID-19 testing centres 19 October to 18 December, 2020	Median age (IQR): 36 (26-50) Sex: 696/1451 (48%) males SYMPTOMS 571/1451 (39%) were symptomatic on the day of testing EXPOSURE 564/1451 (39%) contact with a confirmed case	Eight NPS (0.6%) and 24 saliva samples (1.7%) were not appropriately collected and were not analysed. UNINTERPRETABLE Technical failure led to invalid results in 12 samples (none for nasopharyngeal NAAT, 8 for saliva MGI-2, and 4 for saliva Roche) INDETERMINATE None reported
Klein 2021 Based on NPS RT-PCR: 290 (45)	Single group study. Adults with symptoms suggestive of a SARS-CoV-2 infection or a recent high-risk contact with a confirmed SARS-CoV-2 case presented to a SARS-CoV-2 drive-in testing centre	Germany	AGE & SEX	MISSING DATA
	Recruitment unclear Prospective	COVID-19 testing centre/drive-through 15 December 2020 to 19 January, 2021	Age: mean 42.7 (SD = 14.6) years Sex: 138/290 (47.6%) male SYMPTOMS 133/290 (45.9%) symptomatic EXPOSURE Not reported	One patient with invalid RT-PCR test result was excluded; one with lost written informed consent excluded UNINTERPRETABLE One invalid AgRDT was registered on NP samples, which was valid upon repeat. INDETERMINATE 1 invalid RT-PCR test, the case excluded from the analysis
Kocagoz 2021 363 (114)	363 volunteers above the age of 18, who were admitted to hospital with symptoms of respiratory infection	Turkey	AGE & SEX	MISSING DATA
	Recruitment unclear Prospective	hospital inpatient Not stated	Age: NS Sex: NS SYMPTOMS 363 (100%) symptomatic EXPOSURE Not stated	None reported UNINTERPRETABLE None reported INDETERMINATE None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

Kojima 2020 45 (29)	Two-group study; non-hospitalised adults "recently" tested for COVID-19 as part of a drive-through testing programme	USA Community Not stated	AGE & SEX Median age 42 years (IQR 31 to 52); sex: not stated SYMPTOMS 23 (51%) symptomatic EXPOSURE HX Not stated	MISSING DATA 1 x lost sample UNINTERPRETABLE 2 x insufficient samples INDETERMINATE None reported
	Convenience, Retrospective			
Labhardt 2022 1986 (115)	Single group, 2-site study of adults and children presenting with symptoms compatible with COVID-19 and/or with a history of SARS-CoV-2 exposure meeting pre-defined screening criteria for testing: body temperature $\geq 38^{\circ}\text{C}$ (non-contact forehead thermometer) or reporting at least one of 10 prespecified symptoms or contact to a probable or confirmed COVID-19 case in the last 14 days	Lesotho hospital outpatient 28 December 2020-30 September, 2021	AGE & SEX Age: Median (IQR) 41 years (28-60) of 2131 Sex: 974/2131 (45.7%) male SYMPTOMS 1800/2131 (84.5%) symptomatic EXPOSURE 78/2131 (3.6%) with known exposure to COVID-19 case	MISSING DATA 46/2198 NPS Ag and 88/2093 Nasal ant Ag missing UNINTERPRETABLE None reported INDETERMINATE No Ag results reported as invalid
	Consecutive Prospective			
Landry 2020 124 (35)	Single group; symptomatic outpatients suspected of having COVID-19 attending a drive-through testing site	USA Drive-through COVID-19 testing site April 16 to 28, 2020	AGE & SEX Not stated SYMPTOMS Symptomatic EXPOSURE HX Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
	Consecutive, prospective			
Leung 2020 62 (29) patients 95 (58) samples (analysis)	Single group; patients admitted to hospital Recruitment unclear, Retrospective	China Inpatient February to March, 2020	AGE & SEX Mean age 42 years (SD ± 17.1); 26 (41%) male SYMPTOMS Not stated EXPOSURE HX Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Lindner 2021 (b) 146 (40)	Single-group study Symptomatic adults with high clinical suspicion of SARS-CoV-2, including 1) reported contact with a confirmed case and any compatible symptom, or 2) fever or impaired taste or smell irrespective of exposure	Germany COVID-19 testing centre 30 November to 11 December, 2020	AGE & SEX Mean age 35 years (SD 11.5); 75 (51%) were female SYMPTOMS	MISSING DATA Index and Index reference samples: 4 excluded (3 participants were excluded as they did not fulfil the minimum
	Consecutive			

Table 5. Study design and participant characteristics (a) *(Continued)*

	Prospective		100% symptomatic; Mean duration of pso 3.4 days (SD 2.0) 34 (23%) with comor- bidities	language criterion, 1 participant excluded because of lost PCR specimen)
			EXPOSURE	UNINTERPRETABLE
			Included those with re- ported contact with a confirmed case. No fur- ther details on 'n'	Nasal MT: N = 2 One participant left without reading the test result for nasal sample plus one in- valid result (buffer spilt and test not re- peated)
				INDETERMINATE
				None reported
Lopes 2021 [A&B]	Two single-group cohorts of patients: admitted consecutively to Haematology inpatient ward or healthcare workers with suspected COVID-19 or with close contact with people who tested positive for COVID-19	Brazil	AGE & SEX	MISSING DATA
NP vs OP: 1440 (267)		Mixed: hospital inpatient + HCW	Age: mean (SD): 35.59 (21.82)	1629 NP samples, 1498 saliva samples and 1596 OP samples reported; no reasons for missing samples provided
NP vs Saliva: 1440 (295)		January 2020 to April, 2021	Sex: 690/1683 (41%) male	
NP vs Saliva VTM: 1440 (280)	Consecutive		SYMPTOMS	UNINTERPRETABLE
	Prospective		645/1683 (38.3%) symp- tomatic	None reported
			EXPOSURE	INDETERMINATE
			Not stated	None reported
Mahmoud 2021	Study design unclear	United Arab Emi- rates	AGE & SEX	MISSING DATA
595 (250)	Recruitment unclear	Unclear	Not stated	None reported
	Prospective	Not stated	SYMPTOMS	UNINTERPRETABLE
			Not stated	5 invalid samples for the main analysis
			EXPOSURE	INDETERMINATE
			Not stated	None reported
Marquette 2021 (a); Marquette 2021 (b); Mar- quette 2021 (c)	[1] Mix of symptomatic subjects referred by their attending physician because of recent (≤ 2 weeks) symptoms of COV- ID-19 and close contacts: subjects re- ferred by the contact tracing staff of the French public health insurance	France	AGE & SEX	MISSING DATA
[1] 409 (116)		COVID-19 test- ing centre/dri- ve-through	[a]	None reported
[2] 147 (59)		[1] 21 September 2020 to 8 March, 2021	Age: NS	UNINTERPRETABLE
[3] 262 (57)		[2] 21 September 2020 to 6 Janu- ary, 2021	Sex: 178/409 (44%) male	None reported
		[3] 6 February to 8 March, 2021	[b]	INDETERMINATE
	Consecutive		Age: mean 40 (SD ± 15 years)	None reported
			Sex: 61/147 (42%) male	
			[c]	
			Age: mean 41 (SD ± 15 years)	

Table 5. Study design and participant characteristics (a) *(Continued)*

Prospective			Sex: 117/262 (45%) male	
			SYMPTOMS	
			[a] NS	
			[b] 147/147 (100%) symptomatic	
			[c] NS	
			EXPOSURE	
			[a] NS	
			[b] NS	
			[c] 262/262 (100%) with known exposure to COVID-19 case	
Marx 2021 (a); Marx 2021 (b); Marx 2021 (c); Marx 2021 (d); Marx 2021 (e); Marx 2021 (f)[A&B]	Single group asymptomatic and symptomatic adults enrolled during community testing at homeless service sites and dedicated COVID-19 testing clinics (n = 730)	USA and Georgia	AGE & SEX	MISSING DATA
		Mixed community (homeless and dedicated COVID-19 testing sites)	420/730 (57.5%) male; median age 43	Results for all 3 specimen types available for 1320/1806 (73.1%) participants from Marx [a] and Marx [b]
	Recruitment unclear	August-November, 2020	SYMPTOMS	UNINTERPRETABLE
	Unclear. Probably prospective		269/730 (36.8%)	Insufficient saliva 3%
Nasal ant: 563 (70)			EXPOSURE	INDETERMINATE
Saliva: 496 (60)			159/730 (21.8%) known exposure within 2 weeks	None reported
Marx 2021 (g); Marx 2021 (h); Marx 2021 (i); Marx 2021 (j); Marx 2021 (k); Marx 2021 (l); Marx 2021 (m); Marx 2021 (n); Marx 2021 (o); Marx 2021 (p); Marx 2021 (q); Marx 2021 (r)[A&B]	Single group asymptomatic and symptomatic adults enrolled at clinical settings at a large public hospital (n = 1076)	USA and Georgia	AGE & SEX	MISSING DATA
		Mixed hospital (A&E and 'other')	559/1076 (52%) male; median age 52	Results for all 3 specimen types available for 1320/1806 (73.1%) participants from Marx [a] and Marx [b]
	Recruitment unclear	August-November, 2020	SYMPTOMS	UNINTERPRETABLE
	Unclear. Probably prospective		610/1076 (56.7%)	Insufficient saliva 4.6%
			EXPOSURE	INDETERMINATE
			30/1076 (2.8%) known exposure within 2 weeks	None reported
Nasal: 932 (74)				
Saliva: 864 (69)				
Matic 2020	Single group of patients under investigation for COVID-19 from various clinical settings	Canada	AGE & SEX	MISSING DATA
74 (22)		Mixed (inpatients, residents of long-term care (LTC) facilities, healthcare workers, and outpatients)	Median age (range): 51 (22-95)	None reported
	Unclear "From March–May 2020, paired saliva and nasopharyngeal swabs were received from patients under investigation for COVID-19 from various clinical settings: inpatients, residents of long-term care (LTC) facilities, healthcare workers, and outpatients."	March to May, 2020	Sex: 31/74 (41.9%) male	UNINTERPRETABLE
			SYMPTOMS	31 samples excluded due to insufficient volume and 1 sample because of being a sputum sample
			13/74 (17.6%) symptomatic patients requiring admission to a tertiary acute care hospital	INDETERMINATE

Table 5. Study design and participant characteristics (a) *(Continued)*

	Prospective		13/74 (17.6%) mildly symptomatic outpatients including household contacts of known positive cases	None reported
			EXPOSURE	
			20/74 (27%) LTC residents in outbreak settings and 13/74 (17.6%) outpatients included household contacts of known positive cases	
McCormick-Baw 2020	Unclear; [1] individuals tested on the basis of national or institutional guidelines for COVID-19 (suspected) enriched with cohort [2] tested whilst an inpatient in a COVID-19 unit (presumed D+)	USA	AGE & SEX	MISSING DATA
156 (50)		Mixed inpatient and emergency department	Not stated	None reported
	[1] Recruitment unclear [2] Random, prospective	Not stated	SYMPTOMS	UNINTERPRETABLE
			Not stated	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
McCulloch 2020	[1] Single group; symptomatic health-care workers presenting to drive-through clinics	USA	AGE & SEX	MISSING DATA
158 (18) indeterminate classified +ve	[2] Single group; symptomatic outpatients testing SARS-CoV-2 positive presenting for care in primary care or the ED not included in analysis	Drive-through COVID-19 testing site	Not stated	None reported
158 (14) indeterminate classified -ve.		March 31 to April 13, 2020	SYMPTOMS	UNINTERPRETABLE
	Recruitment unclear,		All symptomatic.	None reported
	Prospective		EXPOSURE HX	INDETERMINATE
			Not stated	1 inconclusive NP swab and 6 inconclusive mid-nasal swabs
McLennan 2022	[1] Single group of NHS Lothian Health Care Workers (HCWs) or their symptomatic household contacts attending the drive through NHS Lothian COVID-19 testing Centre	UK	AGE & SEX	MISSING DATA
109 (11)	[2] Subsample of 19+ and 6- samples from NHS Lothian Health Care Workers (HCWs) or their symptomatic household contacts attending the drive through NHS Lothian COVID-19 testing Centre (not extracted)	COVID-19 testing centre/drive-through	Age: Mean (SD): 40.2 (1.2)	None reported
	[3] Single group of NHS Lothian Health Care Workers (HCWs) or their symptomatic household contacts attending the drive through NHS Lothian COVID-19 testing Centre: Random sample of 37+ and 30- samples (not extracted)	20-22 May, 2020	Sex: 29/109 (26.6%) male	UNINTERPRETABLE
			SYMPTOMS	1 NP/OP and 8 saliva samples had amplification failures.
			Not stated	INDETERMINATE
			EXPOSURE	1 saliva sample inconclusive
	Recruitment unclear		Not stated	
	Prospective			

Table 5. Study design and participant characteristics (a) *(Continued)*

Melo Costa 2021 (a); Melo Costa 2021 (b); Melo Costa 2021 (c) MIXED symptomatic and asymptomatic: 273 (46) Asymptomatic: 183 (17) Symptomatic: 90 (29)	Single group of symptomatic and asymptomatic individuals admitted to the hospital for SARS-CoV-2 routine diagnosis (group of previously tested not extracted for this review) Consecutive (all individuals on demand of SARS-CoV-2 detection using NPS, accepting in parallel, saliva collection) Prospective	France Unclear (hospital setting) 6 October 2020 to 16 October, 2020	AGE & SEX Symptomatic: Median age 41 (IQR 28.3-50.0) 35 (38.9%) male Asymptomatic: Median age 39 (IQR 28.5-49.5) 98 (50.8%) male SYMPTOMS Symptomatic: 90 (33%) EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Mestdagh 2021 (a)[A]; Mestdagh 2021 (a)[B]; Mestdagh 2021 (b)[A]; Mestdagh 2021 (b)[B]; Mestdagh 2021 (c)[A]; Mestdagh 2021 (c)[B] 2469 (118)	Single group Asymptomatic and symptomatic adults (> 18) suggestive of COVID-19 presenting to test triage centres. Laboratory (n = 2850) (Note 104 participants tested not included as NP samples missing) Between June 2020 and July 2020 Prospective	Belgium COVID-19 testing centre Between June 2020 and July 2020	AGE & SEX Age: median age group: 31-40 years old Sex: NS SYMPTOMS 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic EXPOSURE NS	MISSING DATA Missing NP swab results from 104/2850 (3.6%) participants tested Saliva swab samples "not available": 201/2850 (7%). Saliva spit samples "not available": 381/2850 (13%) UNINTERPRETABLE None reported INDETERMINATE None reported
Mestdagh 2021 (d)[A]; Mestdagh 2021 (d)[B]; Mestdagh 2021 (e)[A]; Mestdagh 2021 (e)[B]; Mestdagh 2021 (f)[A]; Mestdagh 2021 (f)[B] 2491 (72)	Single group Laboratory (n = 2526) Between June 2020 and July 2020 Prospective	Belgium COVID-19 testing centre Between June 2020 and July 2020	AGE & SEX NS SYMPTOMS 1376/2071 (%) symptomatic (calculated over 2071) Only 2071 of 2850 included had data on symptom status, of which 1376/2071 (66%) symptomatic EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Migueres 2020 123 (44)	Single group; ambulatory and hospitalised symptomatic and asymptomatic patients	France	AGE & SEX Median age 43 years; 49 (40%) male	MISSING DATA None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

	Recruitment unclear	Mixed inpatient and outpatient numbers	SYMPTOMS	UNINTERPRETABLE
	Unclear if prospective/retrospective	Not stated	Of 44 (36%) with ≥ 1 +ve sample: 17 (39%) asymptomatic, 27 (61%) symptomatic, of which 9/27 (33%) hospitalised	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
Miguères 2021 (a) ; Miguères 2021 (b) ; Miguères 2021 (c)	Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre	France	AGE & SEX	MISSING DATA
301(56)	Recruitment unclear (27 to 29 October, 2020)	COVID-19 testing centre/drive-through	Age: mean 33 (range 3-77 yrs) Sex: 144/303 (47.5%) male (across Miguères 2021 (a) and Miguères 2021 (b))	None reported
	Prospective	27 to 29 October, 2020	SYMPTOMS	UNINTERPRETABLE
			160/303 (52.8%) mildly symptomatic	None reported
			EXPOSURE	INDETERMINATE
			Not stated	2/303 (0.6%) saliva samples provided an indeterminate result.
Miguères 2021 (d) ; Miguères 2021 (e) ; Miguères 2021 (f)	Single group of symptomatic and asymptomatic individuals who came to the Toulouse University Hospital drive-through testing centre	France	AGE & SEX	MISSING DATA
301 (55)	Recruitment unclear (27 to 29 October, 2020)	COVID-19 testing centre/drive-through	Age: Mean 33 (range 3-77 yrs) Sex: 144/303 (47.5%) male (across Miguères 2021 (a) and Miguères 2021 (b))	None reported
	Prospective	27 to 29 October, 2020	SYMPTOMS	UNINTERPRETABLE
			160/303 (52.8%) mildly symptomatic	None reported
			EXPOSURE	INDETERMINATE
			Not stated	2/303 (0.6%) saliva samples provided an indeterminate result.
Miller 2020	Single group; symptomatic and asymptomatic adult participants referred by physicians at two primary care medicine facilities	USA	AGE & SEX	MISSING DATA
91 (36)	Recruitment unclear	Community: referred from primary care	Not stated	None reported
	Mixed prospective and retrospective	Not stated	SYMPTOMS	UNINTERPRETABLE
			Not stated	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
Mora-Aguilera 2022 (a)	2 x single cohorts (a) and (b) of ambulatory volunteers providing paired mouth-	Mexico	AGE & SEX	MISSING DATA
			Age range: 10-81	None reported

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Table 5. Study design and participant characteristics (a) *(Continued)*

23 (9)	pected' COVID-19. Mixed symptomatic and asymptomatic (a third cohort comprising only mouth-wash samples as a part of test development not extracted)	Unclear (including COVID-19 testing centre)	Sex: 30/45 (66%) male (across Mora-Aguilera 2022 (a) and Mora-Aguilera 2022 (b))	UNINTERPRETABLE
	Recruitment unclear	March to June, 2020	SYMPTOMS	None reported
	Prospective		13/45 (28.9%) symptomatic	INDETERMINATE
			EXPOSURE	None reported
			Not stated	
Mora-Aguilera 2022 (b)	2 x single cohorts (a) and (b) of ambulatory volunteers providing paired mouth-wash and NPS samples because of 'suspected' COVID-19 Mixed symptomatic and asymptomatic (a third cohort comprising only mouth-wash samples as a part of test development not extracted)	Mexico	AGE & SEX	MISSING DATA
22 (4)		Unclear (including COVID-19 testing centre)	Age: range: 19-81 Sex: 30/45 (66%) male (across Mora-Aguilera 2022 (a) and Mora-Aguilera 2022 (b))	None reported
	Recruitment unclear	March to June, 2020	SYMPTOMS	UNINTERPRETABLE
	Prospective		13/45 (28.9%) symptomatic	None reported
			EXPOSURE	INDETERMINATE
			Not stated	None reported
Moreno-Contreras 2020	Single-group; primarily ambulatory symptomatic patients attending a respiratory triage centre and who provided paired NP and saliva specimens	Mexico	AGE & SEX	MISSING DATA
71 (34)		Outpatient: ambulatory triage service. 3 samples collected from hospitalised patients	Median age 41 years (SD $\pm$ 14.4); 115 (45%) male	None reported
	Recruitment unclear	2 May to 31 May, 2020	SYMPTOMS	UNINTERPRETABLE
	Unclear retrospective/prospective		Two or more symptoms related to COVID-19	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
Nacher 2021 (a); Nacher 2021 (b)	Single group of persons aged 3 years and older with mild symptoms suggestive of COVID-19 and asymptomatic persons with a testing indication in French Guiana	French Guiana	AGE & SEX	MISSING DATA
1028 (223)		Mixed: hospital outpatients Community and drive-through	453/1028 (44%) males Median age (IQR): 34 (23-47)	n = 56 saliva samples missing or spilled during transport n = 11 NP samples missing or 'not analysed using study protocol'
	Consecutive enrolment of those eligible and consenting	22 July to 28 October, 2020	SYMPTOMS	UNINTERPRETABLE
	Prospective		504/1028 (49%) asymptomatic	N = 6 saliva samples insufficient volume
			EXPOSURE	INDETERMINATE
			277/1028 (26.9%) were contacts of cases.	None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

Otto 2020 92 (49)	Single group; outpatients with symptoms compatible with COVID-19 attending a COVID-19 consultation unit; none had a productive cough	France	AGE & SEX	MISSING DATA
	Recruitment unclear Prospective	COVID-19 testing centre April 2020	Not stated SYMPTOMS All symptomatic, none with productive cough EXPOSURE HX Not stated	None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Pasomsub 2020 200 (21)	Single group; symptomatic adults who either had a history of recent high-risk travel or close contact with a COVID-19 case attending an acute respiratory infection clinic	Thailand	AGE & SEX	MISSING DATA
	Recruitment unclear Prospective	Outpatient 27 March to 4 April, 2020	Median age 36 years (IQR 28-48); 69 (35%) male SYMPTOMS Cough: 108 (54%) Sore throat: 102 (51%) Runny nose: 68 (34%) Sneezing: 26 (13%) Dyspnoea: 73 (37%) EXPOSURE HX Close contact COVID-19 case 170/200 (85%)	None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Patel 2020 146 (25)	Single group; individuals ≤ 7 days post-'illness onset' with paired OP/NP samples	United States	AGE & SEX	MISSING DATA
	Recruitment unclear, Retrospective	Unclear 27 January to 29 February, 2020	Median age 40 years IQR (24-56); 81 (56%) male SYMPTOMS Not stated EXPOSURE HX Not stated	None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Patriquin 2022 392 (64)	Single group of adults recruited from two dedicated COVID-19 testing centres during a four-day period in January of 2022. Meeting eligibility criteria for molecular diagnostic testing by Public Health:	Canada	AGE & SEX	MISSING DATA
	symptomatic or close contact AND - 50 years and over - Unvaccinated - Live or work in congregate settings e.g. residential care, shelters, corrections - HCW - Adults 18-49 with risk factors for severe disease - Children < 18 yrs with risk factors for severe disease - Pregnant - African ethnicity Recruitment unclear	COVID-19 testing centre/drive-through January 2022	All participants were adults. SYMPTOMS Most participants symptomatic or close contact of a known case EXPOSURE Not stated	None reported UNINTERPRETABLE None reported INDETERMINATE None reported

Table 5. Study design and participant characteristics (a) *(Continued)*

Prospective				
Pere 2020 44 (37)	Single group; patients suspected of COVID-19 selected for testing according to medical decision Recruitment unclear, Prospective	France Unclear Up to the end of March 2020	AGE & SEX Median age 63 years (IQR 18-94); 23 (53%) male SYMPTOMS Not stated EXPOSURE HX Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Pham 2020 35 (14)	Single group; symptomatic patients suspected of being infected with SARS-CoV-2 and with three different sample types available (NP, OP, and nasal swabs) Recruitment unclear Unclear prospective/retrospective	United States Unclear Not stated	AGE & SEX Not stated SYMPTOMS All symptomatic EXPOSURE HX Not stated	MISSING DATA Unclear UNINTERPRETABLE None reported INDETERMINATE None reported
Potter 2022 304 (41)	[1] Single group of symptomatic health-care personnel with COVID-19 compatible symptoms and symptomatic patients who met clinical criteria for SARS-CoV-2 and presented to the Emergency Department tested with the Lyra SARS-CoV-2 assay [2] As for [1] but samples tested with different COVID-19 tests. NOT USED IN THIS REVIEW Recruitment unclear Unclear prospective/retrospective	USA Mixed (COVID-19 testing centre (HCW) AND Emergency Department (patients)) 27 April to 20 May, 2020	AGE & SEX Not stated SYMPTOMS All participants included were symptomatic at testing time. EXPOSURE Not stated	MISSING DATA 231/542 samples not included in main analysis because participants were not able to produce enough saliva. UNINTERPRETABLE None reported INDETERMINATE None reported
Procop 2020 224 (42)	Single group; patients with symptoms consistent with COVID-19 (determined by a licenced healthcare provider and reviewed by a second healthcare provider) attending drive-through specimen collection unit Recruitment unclear, Prospective	USA Drive-through COVID-19 testing site Not stated	AGE & SEX Entire cohort (n = 224): mean age 44 years (range 18-82); PCR+ only (n = 39): Mean age 47 years; 14 (36%) male; ethnicity black 19 (49%), white 13 (33%), multiracial 3, (8%), Hispanic 1, other 1, declined 1, unavailable 1 SYMPTOMS All symptomatic EXPOSURE HX	MISSING DATA None reported UNINTERPRETABLE 1 sample no amplification of any N gene target or Rnase P control INDETERMINATE NP: 2 indeterminate (1 or 2 targets amplified), both saliva +ve Saliva: 5 indeterminate, 4 NP -ve (all with only 1 of 3 tar-

Table 5. Study design and participant characteristics (a) *(Continued)*

			Not stated	gets amplified for saliva) and 1 NP +ve (2 of 3 targets amplified for saliva)
Rajh 2021[A]; Rajh 2021[B]; Rajh 2021[C]	[1] Single group of symptomatic and asymptomatic individuals from a public COVID-19 testing site [2] Group of 79 hospitalised COVID-19 patients (population pre-selected- not extracted for this review) [3] Group of 750 individuals with no signs of infection and healthcare workers (not extracted for this review) Recruitment unclear Prospective	Slovenia COVID-19 testing centre Not stated	AGE & SEX Not stated SYMPTOMS Not stated EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Rao 2021(a)	Single group of asymptomatic participants undergoing surveillance testing at Pokok Sena detention centre Unclear: "A cross-sectional two cohort diagnostic study was conducted on candidates who were undergoing surveillance testing for SARS-CoV-2 (...) and amongst asymptomatic travellers arriving at Kuala Lumpur International Airport (KLIA) throughout the month of September 2020". Random participants were asked to provide a deep throat saliva specimen prior to a routine OP/NP sample Unclear prospective/retrospective	Malaysia Other: detention centre 3 October to 10 October, 2020	AGE & SEX Median age 33 (IQR: 25-42) Gender, male: 392 (69.8%) (across Rao 2021(a) and Rao 2021 (b)) SYMPTOMS All participants were asymptomatic at the time of testing. EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Rao 2021 (b)	Single group of asymptomatic travellers arriving at Kuala Lumpur International airport Unclear: "A cross-sectional two cohort diagnostic study was conducted on candidates who were undergoing surveillance testing for SARS-CoV-2 (...) and amongst asymptomatic travellers arriving at Kuala Lumpur International Airport (KLIA) throughout the month of September 2020". Random participants were asked to provide a deep throat saliva specimen prior to a routine OP/NP sample. Unclear prospective/retrospective	Malaysia Other: airport 44,075	AGE & SEX Median age 33 (IQR: 25-42) Gender, male: 392 (69.8%) (across Rao 2021(a) and Rao 2021 (b)) SYMPTOMS All participants were asymptomatic at the time of testing. EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Sahajpal 2021	Unclear group of 240 samples, 95 from a healthcare setting and 145 from a community setting Recruitment unclear	USA Mixed: OP (healthcare cen-	AGE & SEX Not stated SYMPTOMS	MISSING DATA None reported UNINTERPRETABLE

Table 5. Study design and participant characteristics (a) *(Continued)*

(unclear) probably prospective	tre) and commu- nity setting	Not stated	None reported
		EXPOSURE	INDETERMINATE
	Not stated	Not stated	None reported

Abbreviations

AE/A&E: accident and emergency
 Ag: antigen
 Ag NPS: silver nanoparticles
 AgRDT: antigen rapid diagnostic test
 CDC: Centers for Disease Control and Prevention
 CEMIC: Centre for Clinical Medical Education and Research
 COVID-19: coronavirus 19
 CT: computed tomography
 D+: Disease plus
 ED: emergency department
 ER: emergency room
 HCW: healthcare worker
 HX: history
 ICU: intensive care unit
 IGI: Innovative Genomics Institute
 IQR: interquartile range
 LTC: long-term care
 MSKCC: Memorial Sloan Kettering Cancer Centre
 MSU: Michigan State University
 MT: mid-turbinate
 N: number
 nos: not otherwise specified
 NAAT: Nucleic Acid Amplification Test
 NHS: National Health Service
 NOS: not otherwise specified
 NP: nasopharyngeal
 NPS: nasopharyngeal swabs
 NS: not stated
 ONPS: oro-nasopharyngeal swab
 OP: oropharyngeal
 PCR(+): polymerase chain reaction (positive)
 pso: post-symptom onset
 Q: quartile
 RDT: rapid diagnostic tests
 ROC: Receiver Operating Characteristic
 rRT:PCR: reverse real-time reverse-transcriptase polymerase-chain-reaction
 RT-PCR: reverse-transcriptase polymerase-chain-reaction
 SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
 SD: standard deviation
 UCSD: University of California San Diego
 VoC: variant of concern
 WHO: World Health Organization
 yrs: years
 +ve: positive
 -ve: negative

Table 6. Study design and participant characteristics (b)

Study N (SARS-CoV-2 cases)	Design and recruitment	Country setting and dates	Participant characteristics Exposure history Timing of testing	Missing data

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Table 6. Study design and participant characteristics (b) *(Continued)*

				Uninter- pretable/indeter- minate results
Sahni 2021 567 (114)	Single group of symptomatic children attending an outpatient paediatric practice and scheduled for testing Consecutive Prospective	United States of America Hospital outpa- tient 10 April to 31 Ju- ly, 2020	AGE & SEX Age: median (range): 5.0 (0.1-18) Sex: 300/569 (52.7%) male SYMPTOMS Children reported fever and/or ≥ 1 ARI symptom (cough, earache, nasal con- gestion, runny nose, sore throat, wheezing, shortness of breath/rapid or shallow breathing) with onset < 14 days prior to the outpatient visit EXPOSURE Not stated	MISSING DATA 52 excluded for Rnase-P negative or no paired sam- ple taken UNINTER- PRETABLE 2 samples incon- clusive INDETERMINATE None reported
Salvatore 2021 452 (121)	Single group of index cases and their household members enrolled in a household transmission investigation in Utah (UT) and Wisconsin (WI) Consecutive Prospective	USA Contact tracing 22 March to 25 April, 2020	AGE & SEX Age: median (IQR): 27 (18-48); 55/226 (24%) < 18 yrs Sex: 109/226 (48%) males SYMPTOMS 230/454 (51%) symptomatic EXPOSURE Not stated	MISSING DATA None reported UNINTER- PRETABLE None reported INDETERMINATE Specimen pairs in which at least one result was deemed incon- clusive after re- testing or invalid (no signal from ei- ther N1, N2, or RP) were excluded (n = 15 specimens, 14 participants)
Schwob 2020 928 (385)	Single group of adults with "symptoms compatible with COVID-19 according to regional testing criteria" Unclear ("All patients having a result available for the 3 tests were included") Prospective	Switzerland COVID-19 testing centre 25 September to 4 November, 2020	AGE & SEX Age: median (IQR): 31 (25-42) Sex: 473/928 (51%) male SYMPTOMS Symptomatic: 891/928(96%) at least one major symptom and 37/928 (4%) one minor symptom EXPOSURE	MISSING DATA None reported UNINTER- PRETABLE None reported INDETERMINATE None reported

Table 6. Study design and participant characteristics (b) *(Continued)*

			Known exposure to COV-ID-19: 37/928 (4%)	
Senok 2020 401 (35)	Single group of adult patients undergoing COVID-19 testing at the Al Khawaneej Health Center in Dubai, United Arab Emirates (UAE). "Contacts of confirmed positive cases, those with presumptive symptoms with or without history of sure as well as individuals concerned about 'possible infection'" Recruitment unclear Prospective	United Arab Emirates COVID-19 testing centre 29 June to 14 July, 2020	AGE & SEX Age: mean (SD): 35.5 (9.5) Sex: 329/401 (82%) male SYMPTOMS 195/401 (48.6%) asymptomatic EXPOSURE 176/401 (43.9%) with known exposure to COV-ID-19 case	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Skolimowska 2020 132 (19)	Single group; symptomatic healthcare workers (HCWs) and household contacts presenting to a dedicated COVID-19 outpatient clinic and with acute (< 7-day duration) symptoms meeting the Public Health England case definition Recruitment unclear, Prospective	UK COVID-19 testing centre 28 April to 7 May, 2020	AGE & SEX Median age 39 years (IQR 30-51); 43 (33%) male SYMPTOMS Symptomatic "mild community cases" EXPOSURE HX Patients included household contacts and symptomatic HCW.	MISSING DATA None reported UNINTERPRETABLE 1 saliva specimen was inhibited on testing. INDETERMINATE None reported
Smith-Jeffcoat 2021 [A&B] [A] ANS samples: 995 (78) [B] Saliva samples: 921 (73)	Single group of patients from several symptomatic and asymptomatic inpatient and outpatient departments of Grady Memorial Hospital, being tested due to diagnostics (e.g. patients were symptomatic or exposed) or screening (e.g. preoperative requirement or before admission for non-COVID-19 reasons) purposes Consecutive Prospective	USA Mixed: Hospital IP and OP 31 August to 23 November, 2020	AGE & SEX Age: 614/1006 (57.1%) were > 50 years of age Sex: 559/1006 (51.9%) male SYMPTOMS 196/1006 (18.2%) sought care for a COVID-19-related concern; 329/1006 (30.6%) had a chief complaint including COVID-19 symptoms. EXPOSURE Not stated	MISSING DATA 69/1076 NP samples missing and not processed 82/1006 saliva samples not collected or not tested 8/1006 ANS samples not collected or not tested UNINTERPRETABLE None reported INDETERMINATE 1/1076 NP samples indeterminate and excluded for analysis 3/1006 saliva indeterminate and excluded for analysis

Table 6. Study design and participant characteristics (b) *(Continued)*

3/1006 ANS indeterminate and excluded for analysis				
Teo 2021 (a)[A&B] 45 (29)	Single group of migrant workers presenting with symptomatic ARI and asymptomatic roommates of newly diagnosed COVID-19 cases (n = 149) (a) Symptomatic; tested using nasal anterior and saliva samples (n = 45) Prior confirmed cases not included in this review (n = 51). Results of repeated testing of individuals not included in this review. Results of repeated testing of saliva and nasal samples with an alternative RT-PCR test not included in this review. Recruitment unclear Prospective	Singapore Community Between 2 and 26 June, 2020	AGE & SEX Not stated SYMPTOMS 45/45 (100%) symptomatic EXPOSURE None with reported exposure to known COVID-19 case	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Teo 2021 (b)[A&B] 104 (37)	Single group of migrant workers presenting with symptomatic ARI and asymptomatic roommates of newly diagnosed COVID-19 cases (n = 149) (b) Asymptomatic using nasal and saliva samples (n = 104) Prior confirmed cases not included in this review (n = 51). Results of repeated testing of individuals not included in this review. Results of repeated testing of saliva and nasal samples with an alternative RT-PCR test not included in this review. Recruitment unclear Prospective	Singapore Community Between 2 and 26 June, 2020	AGE & SEX Not stated SYMPTOMS 0/104 (0%) symptomatic EXPOSURE 104/104 (100%) with known exposure to COVID-19 case (close contacts)	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
Torres 2021 972 (104)	Paired NP and saliva spit samples from self-reported mild symptomatic or asymptomatic individuals Recruitment unclear Prospective	Arizona COVID-19 testing centre "Community testing sites" Late July to early September, 2020	AGE & SEX Age: mean 34.7 (site 1); 47.8 (site 2) Sex: not stated SYMPTOMS 54/107 (51%) test positives were symptomatic. EXPOSURE Not stated	MISSING DATA None reported UNINTERPRETABLE None reported INDETERMINATE None reported
To 2020 - NP-tongue 501 (49) NP-nasal ant 498 (50) NP-nasal mid 504 (52)	Single group; patients presenting with symptoms indicative of upper respiratory infection at one of five ambulatory clinics Recruitment unclear Unclear prospective/retrospective	USA Outpatient nos 16 to 21 March, 2020	AGE & SEX Age: range 15 months to 94 years: < 30, 116 (23%); 30-39, 116 (23%); 40-49, 92 (18%); 50-59, 87 (17%); ≥ 60, 93 (18%); 201 (40%) male SYMPTOMS	MISSING DATA Unclear UNINTERPRETABLE None reported INDETERMINATE

Table 6. Study design and participant characteristics (b) *(Continued)*

				Of 504 (nasal mid-turbinate vs NP): fever 74 (15%); ear pain/drainage 135 (28%); vomiting 46 (9%); cough 388 (77%); diarrhoea 150 (30%); difficulty breathing 253 (50%).	None reported
				EXPOSURE HX	
				Not stated	
Uddin 2021	Single group of suspected patients (aged > 10 years) and contacts of confirmed COVID-19 cases with or without the signs and symptoms of COVID-19, attending a COVID-19 screening unit	Bangladesh	AGE & SEX	MISSING DATA	
596 (231)		COVID-19 testing centre/drive-through	Age (median- IQR): 32, 26-42 Sex: 338/596 (56.7%) male	None reported	
	Recruitment unclear	July to November, 2020	SYMPTOMS	UNINTERPRETABLE	
	Prospective		546/596 (92%) symptomatic	None reported	
			EXPOSURE	INDETERMINATE	
			Not stated	None reported	
Vaz 2020	Single group; healthcare workers presenting with signs/symptoms suggestive of SARS-CoV-2 infection, and patients at the COVID-19 ward (later described as not hospitalised)	Brazil	AGE & SEX	MISSING DATA	
155 (73)		Outpatient nos	Median age 40 years (IQR 33-48.5); 46 (31%) male	None reported	
	Recruitment unclear	Not stated	SYMPTOMS	UNINTERPRETABLE	
	Unclear prospective/retrospective		All symptomatic ('mild-to-moderate'); no hospitalisations, intubation or deaths; headache (61.2%), cough (45.1%), myalgia (40.3%), sore throat (37.3%), fever (27.6%), anosmia (21.6%), aguesia (20.9%)	None reported	
			EXPOSURE HX	INDETERMINATE	
			Not stated	None reported	
Vermeiren 2020	Single group; COVID-19 symptomatic inpatients, outpatients, and emergency department patients across five hospitals	Canada	AGE & SEX	MISSING DATA	
94 (35)		Mixed inpatients, outpatients, Emergency Department	Not stated	None reported	
	Recruitment unclear	Not stated	SYMPTOMS	UNINTERPRETABLE	
	Prospective		Not stated	(2) Rotor-gene; 1 pair of swabs could not be analysed (disqualified).	
			EXPOSURE HX	INDETERMINATE	
			Not stated	None reported	

Table 6. Study design and participant characteristics (b) *(Continued)*

Villar 2020 13 (9)	Single group; patients with and without liver disease (hepatitis)	Brazil	AGE & SEX	MISSING DATA
	Convenience	Unclear	Not stated	None reported
	Retrospective	Not stated	SYMPTOMS	UNINTER- PRETABLE
			Not stated	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
Vlek 2020 107 (27)	Single group; healthcare workers with symptoms of COVID-19 such as cough, fever, sore throat, dyspnoea, or loss of smell and taste, and within 24 to 48 h of symptom onset	Netherlands	AGE & SEX	MISSING DATA
	Recruitment unclear	Outpatient nos	Median age 34 years (range 19 to 63)	None reported
	Prospective	21 to 29 April, 2020	SYMPTOMS	UNINTER- PRETABLE
			Symptoms of COVID-19 such as cough, fever, sore throat, dyspnoea, or loss of smell and taste	None reported
			EXPOSURE HX	INDETERMINATE
			All HCW	None reported
Walker 2021 225 (20)	Single group of healthcare workers in a variety of roles in inpatient settings who enrolled into the SAFER study, serially sampled with OP/nasal and saliva samples during the 12-week study period.	UK	AGE & SEX	MISSING DATA
	A subgroup of 225 paired (on the same day) samples used for test accuracy estimation in this review. Note: 85 individuals contributed multiple samples.	Other (HCW) in inpatient settings	Age: median (IQR): 35 (27.5-46.5) Sex: 19/85 (22.4) males	None reported
	Recruitment unclear	30 March to 9 April, 2020	SYMPTOMS	UNINTER- PRETABLE
	Retrospective		40/85 (47.1) experienced any symptoms	None reported
			EXPOSURE	INDETERMINATE
			Not stated but some exposed to COVID-19 cases	None reported
Wang 2020 353 (76)	Single group; participants with paired nasopharyngeal and oropharyngeal swabs for diagnosis of SARS-CoV-2 by RT-PCR, including both outpatients (admitted to fever clinic due to COVID-19-like symptoms and fever or chest x-ray abnormality and inpatients (hospital designated for severe and very severe COVID-19 patients)	China	AGE & SEX	MISSING DATA
	Recruitment unclear	Mixed inpatient and COVID-19 testing centre	Median age 54 years (IQR 39-65, range 20 to 88); 176 (50%) male [1] Outpatient median age 49 yrs (IQR 36 to 61, range 20 to 88); 93, 48% male [2] Inpatient median age 61 yrs (IQR 49 to 69, 26 to 87); 83, 52% male	None reported
	Retrospective	16 February to 2 March, 2020	SYMPTOMS	UNINTER- PRETABLE
			All symptomatic with fever and chest x-ray abnormality ± cough and fatigue; outpatient (fever clinic) 192 (54%); inpatient 161 (46%)	None reported

Table 6. Study design and participant characteristics (b) *(Continued)*

			EXPOSURE HX	
			Not stated	
Wehrhahn 2020	Single group; [1] patients presenting for SARS-CoV-2 testing at dedicated COVID-19 collection rooms	Australia	AGE & SEX	MISSING DATA
166 (13)	Single group [2] patients presenting for SARS-CoV-2 testing at dedicated COVID-19 collection rooms not included in the analysis because mean 2.5 days between collection of different sample types	COVID-19 testing centre	Whole cohort 236: median age 40 years (range 9–81); 94 (40%) male	None reported
	Recruitment unclear		SYMPTOMS	UNINTERPRETABLE
	Prospective		Symptomatic ambulatory patients	None reported
			EXPOSURE HX	INDETERMINATE
			Not stated	None reported
Williams 2020	Two-group study; patients presenting to a dedicated COVID-19 screening clinic: [1] All NP +ve	Australia	AGE & SEX	MISSING DATA
89 (40)	[2] Random sample NP -ve	COVID-19 testing centre	Not stated	None reported
	[1] Consecutive NP+	25 March to 1 April, 2020	SYMPTOMS	UNINTERPRETABLE
	[2] Random NP-		Not stated	None reported
	Mixed prospective and retrospective		EXPOSURE HX	INDETERMINATE
			Not stated	None reported
Zander 2021	Close contacts of SARS-CoV-2-positive persons traced by health authorities (n = 80)	Germany	AGE & SEX	MISSING DATA
80 (26)	Most symptomatic at the time of testing	Contact tracing	For RT-PCR positive: Sex: 11/26 (42%) male	Not stated
	Recruitment unclear. Between October and December, 2020	Between October and December, 2020	Age: median 33 (18-89)	UNINTERPRETABLE
	Prospective		For RT-PCR negative: Sex: 21/54 (39%) male	Not stated
			Age: median 30 (13-77)	INDETERMINATE
			SYMPTOMS	None reported
			≥ 73% symptomatic in RT-PCR +ve	
			≥ 69% symptomatic in RT-PCR -ve	
			EXPOSURE	
			80/80 (100%) with known exposure to COVID-19 case, traced by health authorities	

Abbreviations

AE/A&E: accident and emergency

Ag: antigen

AgRDT: antigen rapid diagnostic test

ANS: anterior nasal sample

ant: anterior

ARI: acute respiratory illness

CDC: Centers for Disease Control and Prevention

CEMIC: Centre for Clinical Medical Education and Research

COVID-19: coronavirus-19
 CT: computed tomography
 D+: Disease plus
 ED: emergency department
 HCW: healthcare worker
 h: hour
 HX: history
 ICU: intensive care unit
 IGI: Innovative Genomics Institute
 IP: inpatient
 IQR: interquartile range
 LTC: long-term care
 MSKCC: Memorial Sloan Kettering Cancer Centre
 MT: mid-turbinate
 N 1/2: nucleocapsid gene 1/2
 N: number
 NAAT: Nucleic Acid Amplification Test
 nos: not otherwise specified
 NP +ve: nasopharyngeal positive
 NP -ve: nasopharyngeal negative
 NP/OP: nasopharyngeal/oropharyngeal combined swab
 NPS: nasopharyngeal swabs; NS: not stated
 ONPS: oro-nasopharyngeal swab
 OP: outpatient
 PCR(+/-): polymerase chain reaction (positive/negative)
 NP: nasopharyngeal
 NPS: nasopharyngeal swabs
 NS: not stated
 OP: oropharyngeal
 RP: ribonuclease P
 RT-PCR (+ve/-ve): reverse transcription polymerase chain reaction (positive/negative)
 SAFER: SARS-CoV-2 Acquisition in Frontline healthcare workers - Evaluation to inform Response
 SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
 SD: standard deviation
 UAE:United Arab Emirates
 UT: Utah
 VoC: variant of concern
 vs: versus
 yrs: years
 WI: Wisconsin
 +ve: positive
 -ve: negative

Table 7. Study characteristics: details of testing (index and reference samples) (a)

STUDY N (n SARS-CoV-2 cases)	Index sample details	Index sample test- ing method	Reference sam- ple details	Reference sample testing method
Abdollahi 2020a ; Abdollahi 2020b 50 (28)	(A) Nasopharyngeal	Extraction	(A) Nasopharyngeal (B) Oropharyngeal	Viral Nucleic Acid Extraction kit (Cat. No. YVN50/YVN100) RBC Bioscience, Taipei, Taiwan;
	Device Manufacturer	As for reference index sample	Operator	
	Not stated	Testing method	(A) &(B) Lab technician	Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic Kit (PCR-Fluorescence Probing) of Sansure Biotech (S3102E)
	Operator	As for reference index sample	Collection method	
	Patient			
	Sample Collection	Target		

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Before technicians collected samples, written instructions on how to collect the two required specimens were provided for the patients. Specimens were obtained by a sterile Dacron swab with a plastic handle and soon after collection, each swab was placed into a separate container containing viral transport medium (VTM). Specimens were transported to a clinical laboratory within 30 minutes of collection and processed soon after delivery. (B) Oropharyngeal Device Manufacturer Not stated Operator Patient Sample Collection As for index sample (A)	As for reference index sample Threshold As for reference index sample Threshold predefined Yes	After self-collection (index sample), lab tech collected nasopharyngeal (from opposite nostril) and oropharyngeal samples using a sterile Dacron swab with a plastic handle. Swabs placed into Viral Transport Medium. Specimens transported to a clinical laboratory within 30 minutes of collection and processed soon after delivery	(Changsha, China) and a thermal cycler specified for CFX96™ Real-Time PCR Detection System (Bio-Rad Laboratories, Inc.) Targets Not stated Threshold Ct ≤ 35 Threshold predefined Yes
AbdulRahman 2020a; AbdulRahman 2020b 1009 (60)	Saliva spit Device Manufacturer Saliva collection tube; no details provided Operator Unsupervised patient Collection method Patients were instructed not to drink, smoke or chew gum immediately beforehand. The patient will be instructed to spit into the tube. Saliva production can be helped by placing the tip of the tongue behind the front teeth. Dry/direct sampling Saliva sample can be kept in the fridge for up to 72 hours	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold predefined Yes	Nasopharyngeal swab Operator Not stated Collection method Viral Transport Medium The nasopharyngeal samples were transferred to a viral transport medium immediately after collection and transported to a COVID-19 laboratory for testing; no more details provided	RT-PCR Manufacturer Thermo Fisher Scientific (Waltham, MA) Invitrogen on the Applied Biosystems (Foster City, CA) 7500 Fast Dx RealTime PCR Instrument Extraction Not stated Target E, RdRp and N genes Threshold Ct values > 40 were considered negative. Threshold predefined Yes
Aita 2020 326 (0)	Saliva salivate Device Manufacturer Salivette tubes (SARSTEDT Ag & Co, Numbrecht, Germany)	Extraction As for reference index sample Testing method	Nasopharyngeal Operator Healthcare worker	RT-PCR no further details Targets E gene

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Operator	As for reference index sample	Collection method	Threshold
	Patient			Not stated
	Collection method	Target	Swab no further details	Threshold predefined
	Collect saliva sample immediately before a nasopharyngeal swab. Saliva collected using a cotton swab without preparation. Chew swab for approx one minute to stimulate salivation then return the swab with the absorbed saliva to the Salivette® and replace the stopper.	As for reference index sample		Not stated
		Threshold		
		As for reference index sample		
		Threshold predefined		
	The Salivette® sample was stored at 4 °C immediately after collection and centrifuged at 4000 g for 5 min within 3 h from collection in order to ensure that saliva samples were clear.	Yes		
Akgun Dogan 2021 (a) 200 (98)	(A) Nasopharyngeal	Extraction	Nasopharyngeal/oropharyngeal	SARS-CoV-2 Direct Detection kit (Coyote Bioscience Co, Ltd)
	Device Manufacturer	As for reference index sample		
	Not stated		Operator	Targets
	Operator	Testing method	Healthcare worker	ORF1ab, N genes
	Single, trained healthcare worker	As for reference index sample		Threshold
	Sample Collection	Target	Collection method	Both genes positive; Ct value ≤ 29
	Dacron swab into virus collection tube containing Viral Transport Medium; all samples were transferred to lab within 1 h of sampling and stored in the refrigerator.	As for reference index sample	Not stated	Threshold predefined
		Threshold		Yes
	(B) Oropharyngeal	As for reference index sample		
	Device Manufacturer	Threshold predefined		
	Falcon tube	Yes		
	Operator			
	Single, trained healthcare worker			
	Sample Collection			
	Cotton swab put into falcon tube containing Viral Transport Medium			
	As for sample A (nasopharyngeal)			
	(C) Saliva drool			
	Device Manufacturer			
	Falcon tube			
	Operator			
	Patient			
	Sample Collection			

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Saliva samples collected before nasopharyngeal and oropharyngeal samples. Participants given brief explanation about the difference between saliva and sputum; saliva collected by a drooling technique, spit approx 1 mL into a falcon tube containing Viral Transport Medium; all samples were transferred to lab within 1 h of sampling and stored in the refrigerator.

Al Suwaidi 2021 476 (80)	Saliva spit	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Sterile container	Testing method	Healthcare worker	Allplex 2019-nCoV RT-PCR assay
	Operator	As for reference index sample	Collection method	Extraction
	Unsupervised patient	Target	Not stated	EZ1 DSP Virus Kit (Qia-gen, Hilden, Germany)
	Collection method	As for reference index sample	Unclear (Universal Transport Medium)	Target
	Participants were asked to close their mouths, allow saliva to pool in the mouth for 1 or 2 minutes and then gently spit into the provided sterile container.	Threshold	Nasopharyngeal swab specimens were obtained by trained healthcare personnel using standardised DHA Nasopharyngeal swab collection protocol for COVID-19 screening	N, E and RdRp genes
	Dry/direct sampling	As for reference index sample		Threshold
		Threshold predefined		A cycle threshold (Ct) of 40 was taken as the cut-off for a positive result for the target genes as per the Manufacturer provided protocol.
		Yes		Threshold predefined
				Yes
Altawalah 2020 891 (362)	Salva deep throat	Extraction	Nasopharyngeal swabs	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	A sterile container, not otherwise specified	Testing method	Healthcare worker	TaqPath™ COVID-19 multiplex real-time RT-PCR test
	Operator	As for reference index sample	Collection method	Extraction
	Patient; no details provided	Target	Viral Transport Medium	MagMax Viral/Pathogen Nucleic Acid Isolation Kit (Thermo Fisher Scientific, Waltham, MA, USA)
	Collection method	As for reference index sample	The swab was passed through the nostril until reaching the posterior nasopharynx and removed while rotating.	Target
	Whole saliva (≈1.5 mL) was collected after deep cough from the suspected patients into a sterile patient.	Threshold		ORF1ab, N and S genes
	Viral Transport Medium if viscous	As for reference index sample		
		Threshold predefined		

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

		Yes		Threshold
				Cycle threshold (Ct) values < 37 for three SARS-CoV-2 targets
				Threshold pre-defined
				Yes
Amoo 2021	Nasopharyngeal swab (self-collected)	Extraction	Nasopharyngeal swab (Healthcare worker)	RT-PCR
216 (42)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	As for reference index sample	Testing method	Healthcare worker collected samples. Laboratory-interpreted	Roche COBAS 6800 (Roche Molecular Systems, Rotkreuz, Switzerland)
	Operator	As for reference index sample	Collection method	Extraction
	Supervised patient-collected sample. Laboratory-interpreted.	Target	Transport medium not otherwise specified	Not stated
	Collection method	As for reference index sample	Threshold	Target
	Participants were asked to watch a video noting the procedure, after which they were given swabs and transport medium to collect their samples individually. Participants were monitored both on site by health professionals and remotely using 'Mobihealth consult'. This application allows health professionals to remotely monitor the sample collection process.	As for reference index sample	Collected after self-collected sample. No further details	ORF1ab
		Threshold pre-defined		Threshold
		As for reference index sample		Not stated
				Threshold pre-defined
				Yes
Babady 2021	Oral rinse (sterile water)	Extraction	Nasopharyngeal swabs	RT-PCR
[A&B]	Device Manufacturer	As for reference index sample	Operator	Manufacturer
[1] 98 (35)	Sterile container, no details provided	Testing method	Healthcare worker	Laboratory-developed real-time RT-PCR based on the CDC protocol
[2] 87 (18)	Operator	As for reference index sample	Collection method	Extraction
	Unsupervised patient	Target	Viral Transport Medium	NUCLISENS EasyMag (bioMérieux, Durham, NC)
	Collection method	As for reference index sample	Nasopharyngeal and oropharyngeal swab samples were collected using flocked swabs (CopanDiagnostics, Murrieta, CA) and placed in viral transport media.	Target
	Healthcare workers were asked to place 10 mL of sterile water in their mouth and with mouth closed, swish for 15 seconds, without gargling and spit the water into a sterile container.	Threshold		N1 and N2
	Dry/direct sampling	As for reference index sample		Threshold
	Saliva deep throat	Threshold pre-defined		Samples were considered positive if both analytic targets N1 and N2 were detected.
	Device Manufacturer	Yes		Threshold pre-defined
	Sterile container, no details provided			
	Operator			

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Unsupervised patient			Yes
	Collection method			
	Healthcare workers were first asked to swallow and then bring up saliva from the back of the throat and spit at least 3.0 mL of saliva into an empty sterile container.			
	Dry/direct sampling			
	As for reference index sample			
Banerjee 2021	Saliva drool	Extraction	Nasopharyngeal swab	TMA
110 (59)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
Note, this is an artificial prevalence based on matching cases and non cases to achieve a prevalence of ~ 50%	10 mL conical tube without any transport media	Testing method	Healthcare worker	Aptima SARS-CoV-2 assay
	Operator	As for reference index sample	Collection method	Extraction
	Patient/parent	Target	BD Universal Viral Transport Medium, BD Diagnostics, CA	Not stated
	Collection method	As for reference index sample	Threshold	Target
	Volunteer patients were given a saliva collection kit that included a 9.5" plastic white individually wrapped straw (U.S. Foods, Lenexa, KS) and 10 mL conical tube without any transport media) during their visit at the drive-through test centre and asked to fill their mouth with saliva and use the straw to fill the collection tube with 2 mL of saliva.	As for reference index sample	Respiratory specimen was also collected with a flocked, nylon nasopharyngeal (NP) swab (Jiangsu Hanheng Medical Technology Co., Ltd, China) during the same visit, by the nurse and placed in viral transport media (BD Universal Viral Transport Medium, BD Diagnostics, CA) for SOC testing	ORF1ab gene
	Dry/direct	Threshold pre-defined		Threshold
	Samples were transported to the laboratory by same-day courier (within 8 hours of sample collection) and stored at 4 °C until testing was completed in the clinical laboratory within the next 2 days (except 4 specimens that were tested between 2 and 5 days from collection).	Yes		Not stated
				Threshold pre-defined
				Yes
Becker 2020	Saliva spit	Extraction	Nasopharyngeal	RT-PCR
88 (17)	Device Manufacturer	MagMax Viral/Pathogen RNA purification kit (ThermoFisher CAT: A42352)	Operator	Manufacturer
	Random allocation to either the Oragene OGD-610 DNA collection kit (55/88) and Orasure OM-505 Microbiome collection kit (33/88)	Testing method	Not stated	CDC RT-PCR assay
	Operator	UCSD TaqPath Multiplex RT-PCR COV-ID-19 assay OR He-lix Primerdesignv1	Collection method	Extraction
	Patient		Swab	Not stated
	Collection method		Sent for testing at the Nevada State Public Health Testing Laboratory	Targets
	Proprietary nucleic acid stabilisation solution added by patient to saliva sam-	Targets		Not stated
				Threshold

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	ple for both collection devices. Shipped overnight for testing at a high complexity CLIA laboratory. Samples were aliquoted upon receipt and immediately processed. Additional aliquots were stored at -20 °C for subsequent processing.	Taqpath: N; ORF 1ab; S Primer: RdRp; PD-IEC	ry. No further details	Positive for any gene target
		Threshold		Threshold pre-defined
		Positive for any gene target		Yes
		Threshold pre-defined		
		Yes		
Begum 2022	Nasal not otherwise specified	Extraction	Nasopharyngeal	RT-PCR
214 (112)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated		Not stated	RT-PCR
	Operator	Testing method	Collection method	Extraction
	Not stated	As for reference index sample	Viral Transport Medium	Chemagic viral NA/gDNA kit (PerkinElmer, MA, USA)
	Collection method	Target	Not stated	Target
	Viral Transport Medium	As for reference index sample		ORF1ab (RdRp)
	No further details	Threshold		Threshold
		As for reference index sample		Ct > 30
		Threshold pre-defined		Threshold pre-defined
		Yes		Yes
Benoit 2021	Spring water gargle	Extraction	Mixed Nasopharyngeal/oropharyngeal	RT-PCR
647 (134)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Globet (ESKA®, St-Mathieu-d'Harricana)	Testing method	Healthcare worker (HCW)	The Cobas® SARS-CoV-2 test on the Cobas® 6800 in St-Eustache (n = 300) and the Cobas® 8800 in Montreal (n = 347)
	Operator	As for reference index sample	Collection method	Extraction
	Unsupervised patient	Target	PCR media not otherwise specified	Not stated
	Collection method	As for reference index sample	Oropharyngeal/nasopharyngeal was collected by a trained healthcare professional by swabbing the posterior oropharynx and then insert-	Target
	Collected after nasopharyngeal /oropharyngeal swabs. Participants were asked not to eat, drink, or smoke for 15 min before. They were handled a goblet with 5 mL of natural spring water (ESKA®, St-Mathieu-d'Harricana) and were told to gargle with the water for 5 s in the mouth, 5 s in the throat, to repeat this process once and then to spit as much as possible in the initial goblet. They were then asked to transfer their gargle specimen into a	Threshold		ORF1ab and E genes
		As for reference index sample		Threshold
		Threshold pre-defined		Samples were considered positive if they met the interpretation
		Yes		

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Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	tube that was sent to a designated laboratory for processing and testing. Natural spring water. Gargle specimens were split in the laboratory as follows: 1 mL was added to 4.3 mL of PCR media and 400 µl was added to 200 µl of Cobas® Omni Lysis Reagent for 10 min.		ing the same swab through one nostril and rotating for 5–10 s before removing.	criteria of the manufacturer. Threshold pre-defined Yes
Bhattacharya 2021 74 (58)	Saliva not otherwise specified Device Manufacturer Not stated Sample Collection Patient Saliva specimens collected in sterile sputum containers transported as 'per standard guidelines'	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined As for reference index sample	Nasopharyngeal Operator Not stated Collection method Swab. No further details	QIAamp Viral RNA Mini Kit (Qiagen); Cobas 6800 (Roche Molecular Diagnostics, Pleasanton, CA, USA) Targets ORF1, E genes Threshold Both genes positive or ORF1 positive Threshold pre-defined Not stated
Bidkar 2022 80 (40)	Saliva swab Device Manufacturer Not stated Operator Supervised patient Collection method The suspect was asked to give a gentle external message to the submandibular gland region from outside for a period not less than 60 s. A broad-ended flocked Nylon swab stick was rolled on the floor of the oral cavity for 20–40 s by the suspect himself/herself. Viral Transport Medium	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined As for reference index sample	Mixed Nasopharyngeal/oropharyngeal Operator Healthcare worker Collection method Viral Transport Medium conventional nasopharyngeal- oropharyngeal swabs of suspects were collected by trained healthcare workers using Nylon swab sticks and transferred to viral transport medium (VTM) as per guidelines laid by statutory bodies.	RT-PCR Manufacturer A SARSCoV-2 Nucleic Acid Diagnostic Kit, no details provided Extraction Labsystem RT-PCR kit Target ORF1ab and E genes Threshold The cycle threshold (Ct) values of both target genes was ≤ 38. Threshold pre-defined Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Bikos 2021 243 (70)	Saliva spit	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer SalivirDetect: 50 mL centrifuge tube Operator Unsupervised patient Collection method Approx. 5 mL of saliva was collected in a 50 mL centrifuge tube; no other details provided	The tube was placed in a 95 °C oven (Fisherbrand Isotemp General Purpose Heating and Drying Oven) for 45 min, then allowed to sit at room temperature to cool. Testing method NEB Luna Kit Target N1 genes Threshold Not stated Threshold pre-defined Not stated	Operator Not stated Collection method Not stated	Manufacturer Real-time PCR thermocycling was performed per CDC guidelines; no details provided Extraction Plates were covered with sealing foil and heated to 95 °C for 5 min in a standard thermocycler then cooled to 4 °C. Target N1, N2, and RNPS genes Threshold Not stated Threshold pre-defined Not stated
Boerger 2021 (A&B) 281 (35)	Saliva spit	Extraction	Nasopharyngeal	RT-PCR
	Device Manufacturer OMNIgene-ORAL (OM-505) collection kit (DNA Genotek, Ottawa, Ontario, Canada) Operator Unsupervised patient Collection method OMNIgene-ORAL (OM-505) collection kit (DNA Genotek, Ottawa, Ontario, Canada) OMNIgene-ORAL (OM-505) collection kit (DNA Genotek, Ottawa, Ontario, Canada) Nasal mid-turbinate Device Manufacturer Not stated Operator Unsupervised patient Collection method	NucliSENS EMAG (bioMérieux; Durham, NC), the Hamilton Micro-lab STAR (Hamilton; Reno, NV) or the MagNA Pure 96 (Roche; Indianapolis, IN) Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined: As for reference index sample	Operator Healthcare worker Collection method Routine protocol, no details provided	Manufacturer Mayo Clinic laboratory-developed test Extraction NucliSENS EMAG (bioMérieux; Durham, NC) or the Hamilton Micro-lab STAR (Hamilton; Reno, NV) Target N gene Threshold Not stated Threshold pre-defined No, selective re-testing of discordant results

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

Patients used a flocked MT swab (Copan Diagnostics, Murrieta, CA) specimen from both nostrils.		Extraction NucliSENS EMAG (bioMérieux; Durham, NC) or the Hamilton Microlab STAR (Hamilton; Reno, NV)
		Testing method As for reference index sample
		Target As for reference index sample
		Threshold As for reference index sample
		Threshold predefined As for reference index sample

Borghi 2021a; Borghi 2021b 192 (87)	Saliva salivate	Extraction As for reference index sample	Nasopharyngeal swab	RT-PCR
	Device Manufacturer		Operator	Manufacturer
	Sterile 50 mL tube		Not stated	A qPCR using N1 (FAM, BHQ-1 labelled probe) and RP (Cy5, BHQ-1) primers/probes published by the Center for Disease Control and Applied Biosystem 7500 Fast instrument
	Operator		Collection method	
	Patient/parent; no details provided		Not stated	
	Collection method			
	A sterile dental cotton roll was kept for two minutes in the vestibular space next to the lower premolar-molar area, then under the tongue close to the Wharton duct opening for additional two minutes. Once duly soaked with saliva, the dental roll was preserved in a sterile 50 mL tube, at room temperature until use (up to 7 days).	Target As for reference index sample		
		Threshold As for reference index sample		Extraction Not stated
		Threshold predefined As for reference index sample		Target N1 and RP primers
				Threshold Samples were considered positive upon detection of N1 (Ct < 40).
				Threshold predefined Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Borghi 2021c	Saliva salivate	Extraction	Nasopharyngeal swab	RT-PCR
109 (27)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Sterile 50 mL tube	Testing method	Not stated	A qPCR using N1 (FAM, BHQ-1 labelled probe) and RP (Cy5, BHQ-1) primers/probes published by the Center for Disease Control and Applied Biosystem 7500 Fast instrument
	Operator	As for reference index sample	Collection method	
	Patient/parent; no details provided	Target	Not stated	
	Collection method	As for reference index sample		Extraction
	A sterile dental cotton roll was kept for two minutes in the vestibular space next to the lower premolar-molar area, then under the tongue close to the Wharton duct opening for additional two minutes. Once duly soaked with saliva, the dental roll was preserved in a sterile 50 mL tube, at room temperature until use (up to 7 days)	Threshold		Not stated
		As for reference index sample		Target
	Threshold predefined			N1 and RP primers
	Dry/direct sampling	As for reference index sample		Threshold
				Samples were considered positive upon detection of N1 (Ct < 40).
				Threshold predefined
				Yes
Boutros 2021(a)	Saliva salivate	Extraction	Nasopharyngeal swab	RT-PCR
147 (59)	Device Manufacturer	No RNA extraction	Operator	Manufacturer
	Small hydroxylated polyvinyl acetate (PVA) sponges; Meroce [®] Standard Dressing, réf 400400; Medtronic, Dublin, Ireland	Testing method	Not stated	RT-PCR,
	Operator	RT-PCR	Collection method	Da An Gene DA0992-Detection Kit for 2019-nCoV (Da An Gene Co., Ltd., Sun Yat-sen University, Guangzhou, China) Idylla SARS-CoV-2 test cartridges (reference A1043/6; Biocartis, Mechelen, Belgium)
	Supervised patient ("All 409 participants performed the salivary self-sampling with the OS correctly as explained.")	Da An Gene DA0992-Detection Kit for 2019-nCoV (Da An Gene Co., Ltd., Sun Yat-sen University, Guangzhou, China) Idylla SARS-CoV-2 test cartridges (reference A1043/6; Biocartis, Mechelen, Belgium)	Viral Transport Medium (VTM)	Extraction
	Collection method	Target	Swabs were eluted into a vial containing viral transport medium	Not stated
	Sponges were placed in the mouth for 1 minute and inserted into a sterile collection tube by the subjects themselves. No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette	As for reference index sample	Oropharyngeal and nasopharyngeal sampled in random order	Target
	Oropharyngeal and nasopharyngeal	Threshold		N, Orf1b genes
	sampled in random order.	As for reference index sample		Threshold
	Dry/direct sampling			N and/or Orf1b genes ≤ 36
		Threshold predefined		Threshold predefined

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

		As for reference index sample	Yes
Boutros 2021 (b)	Saliva salivate	Extraction	Nasopharyngeal swab
262 (57)	Device Manufacturer	No RNA extraction	Manufacturer
	Small hydroxylated polyvinyl acetate (PVA) sponges; Meroce [®] Standard Dressing, réf 400400; Medtronic, Dublin, Ireland	Testing method	TMA; no further details
	Operator	TMA; no further details	Extraction
	Supervised patient ('All 409 participants performed the salivary self-sampling with the OS correctly as explained.')	Target	Not stated
	Collection method	As for reference index sample	Target
	Sponges were placed in the mouth for 1 minute and inserted into a sterile collection tube by the subjects themselves. No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette	Threshold	N, Orf1b genes
	Oropharyngeal and nasopharyngeal sampled in random order	Threshold predefined	Relative light unit (RLU) above 850 for TMA
	Dry/direct sampling	As for reference index sample	Threshold predefined
			Yes
Bruxvoort 2021 [A&B]	Saliva	Extraction	Mixed Nasopharyngeal/oropharyngeal
2112 (335)	Device Manufacturer	As for reference index sample	Manufacturer
	SpectrumDNA [™] saliva collection Device (Spectrum Solutions, Draper, UT)	Testing method	Healthcare worker
	Operator	As for reference index sample	Collection method
	Supervised patient	Target	Viral Transport Medium
	Collection method	As for reference index sample	nasopharyngeal/oropharyngeal specimens were collected by nurses using a long, thin swab to swab the back of the throat, avoiding the tongue, followed by inserting the same swab into one nostril parallel to the palate for a few seconds to absorb nasopharyngeal secretions.
	Per manufacturer instructions, patients were asked to 1) provide approximately 2 mL of spit into the collection tube measured by a standardised wavy black line, 2) screw on a separate cap to release a stabilising solution, and 3) shake for 5 s	Threshold	Extraction
	Dry/direct sampling	As for reference index sample	Not stated
	As for reference index sample	Threshold predefined	Target
	Nasal anterior nares	As for reference index sample	ORF1ab and E genes
	Device Manufacturer		Threshold
	A tube with Viral Transport Medium; no details provided		Not stated
	Operator		Threshold predefined
	Supervised patient		Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Collection method				
Anterior nares swabs were collected by asking the patient to insert a shorter, thicker swab less than 1 in. into the nostril, rotate the swab against the nostril wall several times, and repeat with the other nostril.				
Viral Transport Medium				
Callahan 2021(a); Callahan 2021(b); Callahan 2021(c); Callahan 2021(d) [1] Initial (general): 196 (35) This was calculated by adding up TP, FN and FP for shallow and deep nasal samples combined in the initial tested group	Nasal anterior nares (- shallow method)	Extraction	Nasopharyngeal	RT-PCR
	Device Manufacturer	As for the reference index sample	Operator	Manufacturer
	Collection tube	Testing method	Healthcare worker	Abbott RealTime SARS-CoV-2 assay for EUA
	Operator	As for the reference index sample	Collection method	Extraction
	Healthcare worker	Target	3ml Viral Transport Medium	Not stated
	Collection method	As for the reference index sample	The nasopharyngeal swab used was the Copan BD ESwab collection and transport system swab, with a head of flocked nylon (catalog no. 220532; Copan Diagnostics, Inc., Murietta, CA). "Standard swab procedure"	Target
	The nasal swab used was the included Abbot swab for the GITS arm and the Hologic Aptima multitest swab otherwise (catalog no. AW-14334-001-003; Hologic, Inc., Marlborough, MA), all with polyester/nylon/rayon spun material. The swab tip was inserted into the nostril, the patient was told to press a finger against the exterior of that naris, and the swab was rotated against this external pressure for 10 seconds; this procedure was repeated with the same swab on the other naris.	Threshold		RdRp and N genes
	Modified CDC viral transport medium (VTM) (Hanks' balanced salt solution containing 2% heat-inactivated foetal bovine serum [FBS], or GITS or DRY	As for the reference index sample		Threshold
	Nasal-mid-turbinate (deep method)	Threshold predefined		Positivity: above the reporting threshold of 31.5
	Device Manufacturer	As for the reference index sample	Extraction	Threshold predefined
	Collection tube	Not stated		Yes
	Operator	Testing method		
	Healthcare worker	As for reference index sample		
	Collection method	Target		
	The nasal swab used was the included Abbot swab for the GITS arm and the Hologic Aptima multitest swab otherwise (catalog no. AW-14334-001-003; Hologic, Inc., Marlborough, MA), all with polyester/nylon/rayon spun material. The swab was inserted into the naris until re-	As for reference index sample		
		Threshold		
		Positivity: above the reporting threshold of 31.5		
		Threshold predefined		
		As for reference index sample		

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	distance was felt, and the swab was then rotated for 15 seconds without external pressure (Figure S1b); this procedure was repeated with the same swab on the other naris. Modified CDC viral transport medium (VTM) (Hanks' balanced salt solution containing 2% heat-inactivated foetal bovine serum [FBS], OR GITC OR dry			
Callahan 2021(e)	Saliva spit	Extraction	Nasopharyngeal swab	RT-PCR
Initial assessment: 343 (68)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Sterile sample collection cup (VWR International; part no. 76299-868)	Testing method	Healthcare worker	Abbott m2000 RealTime SARS-CoV-2 assay on an Abbott m2000 RealTime system ("m2000") or the Abbott Alinity m system ("Alinity").
	Operator	As for reference index sample	Collection method	
	Unsupervised patient	Target	Viral Transport Medium	
	Collection method	As for reference index sample	Nasopharyngeal swab was inserted into the nasopharynx and rotated for 10 s.	Extraction
	While waiting in line for nasopharyngeal testing, each participant was given a sterile sample collection cup (VWR International; part no. 76299-868) and asked to spit/drool into a clearly labelled 3 mL fill line. No exclusions were made on the basis of recent consumption of food or drink or of smoking, and participants were not asked to rinse the mouth or perform any other preparation ahead of sample collection. They were informed that 3 mL is a large amount of saliva and may take several minutes/deposits to achieve and that thinking of a favourite food may help trigger salivation.	Threshold		Not stated
		As for reference index sample		Target
		Threshold predefined		Not stated
		As for reference index sample		Threshold
				Cut-off for positive was a Ct value of 31.5 on the m2000 and 42 on the Alinity m.
				Threshold predefined
	Dry/direct sampling			Yes
Castelain 2021	Saliva swab	Extraction	Nasopharyngeal swab	RT-PCR
501 (26)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated	Testing method	Healthcare worker	Abbott RealTime SARS-CoV-2 assay
	Operator	As for reference index sample	Collection method	Extraction
	Healthcare worker	Target	Viral Transport Medium	Automated sample preparation using magnetic microparticles (Abbott mSample Preparation System DNA)
	Collection method	As for reference index sample	Not stated	
	The saliva sample was collected by swabbing the fluid in the groove at the base of the lower jaw.	Threshold		Target
	Viral Transport Medium			

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

		Not stated		RdRp and N genes
		Threshold pre-defined		Threshold
		As for reference index sample		Not stated
				Threshold pre-defined
				Yes
Chu 2021 (a) [A&B] 300 (33)	Saliva swab	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated	Testing method	Healthcare worker	RT-PCR no targeting the S gene; no further details provided
	Operator	As for reference index sample	Collection method	Extraction
	Supervised patient	Target	Not stated	Not stated
	Collection method	As for reference index sample		Target
	Not stated	Threshold		Not stated
	Nasal mid-turbinate	As for reference index sample		Threshold
	Device Manufacturer	As for reference index sample		Not stated
	Not stated	Threshold pre-defined		Threshold pre-defined
	Operator	As for reference index sample		Not stated
	Supervised patient			
	Collection method			
	Not stated			
Chu 2021 (b) [A&B] 107 (40)	Saliva swab	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated	Testing method	Healthcare worker	RT-PCR no targeting the S gene; no further details provided
	Operator	As for reference index sample	Collection method	Extraction
	Supervised patient	Target	Not stated	Not stated
	Collection method	As for reference index sample		Target
	Not stated	Threshold		Not stated
	Nasal mid-turbinate	As for reference index sample		Threshold
	Device Manufacturer	As for reference index sample		Not stated
	Not stated	Threshold pre-defined		Threshold pre-defined
	Operator	As for reference index sample		Not stated
	Supervised patient			
	Collection method			
	Not stated			

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Congrave-Wilson 2021 889 (584)	Saliva spit	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	50 mL sterile container	Testing method	Healthcare worker	CDC protocol for RT-PCR
	Operator	As for reference index sample	Collection method	Extraction
	Unsupervised patient	Target	Universal Transport Medium	QIAamp Viral RNA Mini Kit (QIAGEN, Valencia, CA)
	Collection method	As for reference index sample	Study staff obtained the nasopharyngeal swab specimen following CDC guidelines; no details provided	Target
	Participants self-collected 3 mL of saliva by allowing saliva to collect in the mouth and then dribbling or gently spitting into a 50 mL sterile container. They were also instructed not to cough or clear their throat while providing the saliva samples to avoid contamination with excessive mucus.	Threshold		N1 and N2 genes
	No preservative was added.	As for reference index sample		Threshold
		Threshold pre-defined		Cycle threshold (Ct) value less than 40 for both N1 and N2
				Threshold pre-defined
				Yes
Cradic 2020 182 (12)	(A) Oropharyngeal	Extraction	Nasopharyngeal	Abbott ID NOW COVID-19 assay (Abbott Diagnostics)
	Device Manufacturer	As for reference index sample	Operator	Targets
	Not stated	Testing method	Healthcare worker	RdRp
	Sample collection	As for reference index sample	Collection method	Threshold
	Healthcare worker	Target	Flocked swab	Not stated
	Dry swab no further details	As for reference index sample	Swabs were placed into 3 mL of sterile UVT (Becton Dickinson). Specimens were tested as soon as possible after collection, or if testing was delayed, were stored for up to 72 hours at 2 °C to 8 °C.	Threshold pre-defined
	(B) Nasal not otherwise specified	Threshold		Yes
	Device Manufacturer	As for reference index sample		
	Not stated	Threshold pre-defined		
	Sample collection	As for reference index sample		
	Healthcare worker.			
	Collected according to CDC instructions using a single dry swab to sample both nares			
	Swabs placed into 3 mL of sterile UVT (Becton Dickinson). Specimens were tested as soon as possible after collection, or if testing was delayed, were stored for up to 72 hours at 2 °C to 8 °C.			

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Da Silva 2022	Saliva not otherwise specified	Extraction	Nasopharyngeal swab	RT-PCR
61 (19)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated		Healthcare worker	Allplex™ 2019-nCov Assay (Seegene) kit
	Operator	Testing method	Collection method	Extraction
	Supervised patient	As for reference index sample	Saline solution	Bio Gene Kit from Bio-clin
	Collection method	Target	No further details	Target
	Patients self-collected were 'guided' in collection of saliva samples in sterile containers.	As for reference index sample		RdRP, N, and E genes
	No Transport Medium	Threshold		Threshold
		As for reference index sample		At least one of the target genes amplified at Ct < 40
		Threshold pre-defined		Threshold pre-defined
		As for reference index sample		Yes
De Oliveira 2021	Saliva spit	Extraction	Mixed Nasopharyngeal/oropharyngeal	RT-PCR
400 (157)	Device Manufacturer	No RNA extraction; saliva specimens were thawed at room temperature, vortexed and a 50 µL aliquot was transferred to a 96 wells plate and 60 µg of proteinase K (New England Biolabs, USA) were added.	Operator	Manufacturer
	Dry sterile container		Healthcare worker	At availability: A lab-developed test (LDT) (n = 361), the Cobas® SARS-CoV-2 test in a Cobas 6800 system (Roche Diagnostics, USA) (n = 32) or the Abbott RealTime SARSCoV-2 assay (Abbott, USA) (n = 10)
	Operator		Collection method	Extraction
	Unsupervised patient/parent		3 mL of 0.9 % saline solution	For LDT RT-PCR assay: Chemagen magnetic bead technology on the Chemagic™ 360 instrument (PerkinElmer, USA)
	Collection method	Testing method	Two oro/nasopharyngeal swabs (oropharyngeal swabs) were collected: one was introduced into the throat and scraped for 10 s and the second was into the nose and scraped for 10 s in each nostril.	Other RT-PCR: Not stated
	Patients were previously instructed to avoid drinking water for 10 min and refrain from other drinks, food, and nasal sprays for half an hour before sample collection. Patients received a dry sterile container and were asked to concentrate the saliva in their mouth and spit it (~1 mL) in the container and close it.	Protocol T: Taq-Path™ COVID-19 CE-IVD RT-PCR kit (ThermoFisher Scientific, USA)		Target
	Dry/direct sampling	Target		For LDT: E gene
	Specimens were stored at -20 °C until processed (4 h to 3 days)	Protocol T: S, N and ODRF1ab genes		Other assays: Not stated
		Threshold		Threshold
		The sample is considered positive for SARS-CoV-2 if two or more targets amplify or if only gene N amplifies at a Ct threshold ≤ 40, as		The sample is considered positive for SARS-CoV-2 if two or more targets amplify or if

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

		determined during our validation process. Samples in which only gene S or ORF1ab was positive, were considered negative for SARS-CoV-2.		only gene N amplifies at a Ct threshold ≤ 40 .
		Threshold pre-defined		Threshold pre-defined
		Not stated		Yes
Desai 2021(a)[A]; Desai 2021(a)[B]; Desai 2021(a)[C]	Nasal anterior nares	Extraction	Nasopharyngeal	Real-time reverse transcription isothermal amplification test (iAMP)
	Device Manufacturer	As for reference index sample	Operator	atilabiosystems.com/our-products/covid-19/
From extracted 2x2 tables taking the sample pairs with the most D+ on either sample pair: 117 (16)	Not stated	Testing method	Healthcare worker	Collection method
	Operator	As for reference index sample		Dry/direct sampling
	Unsupervised patient	Target	Not stated	Manufacturer
	Collection method	As for reference index sample		Atila iAMP test
	Not stated	Threshold		Extraction
	Dry/direct sampling	As for reference index sample		No RNA extraction
	samples frozen at -80 °C	Threshold pre-defined		Target
	Saliva not otherwise specified	As for reference index sample		N and ORF1ab genes
	Device Manufacturer	Threshold pre-defined		Threshold
	Not stated	As for reference index sample		Positive: if an exponential amplification curve with a cycle threshold (Ct) of 50 was present in the FAM (ORF1ab or N genes) channel
	Operator			Threshold pre-defined
	Unsupervised patient			Yes
	Collection method			
	Dry/direct sampling			
	samples frozen at -80 °C			
	No further details			
Desai 2021(b)	Saliva not otherwise specified	Extraction	Nasopharyngeal	Real-time reverse transcription isothermal amplification test (iAMP)
	Device Manufacturer	As for reference index sample	Operator	atilabiosystems.com/our-products/covid-19/
From extracted 2x2 tables taking the sample pairs with the most D+ on either sample pair: 1153 (230)	Not stated	Testing method	Healthcare worker	Collection method
	Operator	As for reference index sample		[El Salvador] Dry/direct sampling
	Unsupervised patient	Target		[Paraguay] Viral Transport Medium
	Collection method	As for reference index sample		No further details
	Not stated			Manufacturer
	Dry/direct sampling			Atila iAMP test
				Extraction
				No RNA extraction

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

[El Salvador] Not stated [Paraguay] samples frozen at -20 °C		Threshold		Target
		As for reference in- dex sample		N and ORF1ab genes
		Threshold prede- fined		Threshold
		As for reference in- dex sample		Positive: if an expo- nential amplifica- tion curve with a cy- cle threshold (Ct) of 50 was present in the FAM (ORF1ab or N genes) channel
				Threshold prede- fined
				Yes
Desmet 2020	Oropharyngeal/nasal mid-turbinate	Extraction	Nasopharyngeal	NucliSens easyMag
36 (35)	Device Manufacturer	As for reference in- dex sample	Operator	RNA extraction (bio- Merieux, Marcy-l 'Etoile, France);
	Not stated		Not stated	
	Sample collection	Testing method	Collection method	One-step RT-PCR (Qia- gen One Step RT-PCR kit, Qiagen, Hilden, Germany)
	Not stated	As for reference in- dex sample	Nasopharyngeal "flexible mini tip flocked swab" performed after oropharyngeal/n in order not to contaminate the mid-turbinate part of the nose with viral materia from the nasopharynx Swabs rotated x 3 for 'optimal mu- cosal contact'	Targets
	"Non-flexible flocked swab with normal tip" rubbed in the oropharyngeal space twice at both sides of the uvula and the same swab placed into both nasal cavi- ties until resistance felt. Swabs rotated x 3 for 'optimal mucosal contact'	Target		Not stated
	Amies transport medium	As for reference in- dex sample		Threshold
		Threshold prede- fined		Ct < 50
		As for reference in- dex sample		Threshold prede- fined
			Amies transport medium or uni- versal transport medium (UTM)	Yes
Dumaresq 2021	Gargle with natural spring water	Extraction	Mixed oropharyn- geal/nasopharyn- geal	RT-PCR
1005 (129)	Device Manufacturer	As for reference standard sample		Manufacturer
	15 mL conical polypropylene centrifuge tube	Testing method	Operator	Allplex™ 2019-nCoV Assay kit on CFX96
	Operator	As for reference standard sample	Healthcare worker	Touch Real-Time PCR Detection System (Bio-Rad, Hercules, CA, USA)
	Supervised patient	Target	Collection method	Extraction
	Collection method	As for reference standard sample	The oropharyn- geal/ nasopharyn- geal	No RNA extraction
	Participants were then provided with 5 mL of natural spring water (Eska water, St Mathieu d'Harricana, Quebec, Canada)	Threshold		

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	da or Naya water, Mirabel, Quebec, Canada) in a disposable soft plastic cup (Plastic Medicine Cups, AMG Medical, Montreal, Quebec, Canada) and instructed to rinse their mouth for 5 s, tilt their head back and gargle for 5 s, repeat this cycle once, expel the water back in the plastic cup and empty it in a 15 mL conical polypropylene centrifuge tube.	As for reference standard sample	swab was placed in a conical 15 mL centrifuge tube containing 3 mL of molecular water (PCR grade water)	E, RdRp and N genes
	Natural spring water	Threshold predefined	The flocked swab was first used to swab the posterior oropharynx and the tonsillar arches, and then the same swab was inserted through one nostril parallel to the palate until resistance was met or the distance was equivalent to the distance from the patient's ear to their nostril, rotated several times and left in place for 5–10 s prior to being removed.	Threshold Ct values; no details provided
	The specimens were refrigerated at the collection site and transported to the laboratory in insulated coolers with ice packs.	As for index reference sample		Threshold predefined No, selective retesting of discordant and invalid samples
Echavarria 2021	Saliva not otherwise specified	Extraction	Nasopharyngeal	RT-PCR
174 (64)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Plastic sterile container	Testing method	Healthcare worker	Optimised in-house one-step realtime RT-PCR assay
	Operator	As for reference index sample	Collection method	Extraction
	Unsupervised patient	Target	2 mL viral transport media (Minimun Essential Medium; Gibco)	Quick-RNA™ Viral Kit, Zymo Research Corp
	Collection method	As for reference index sample	Not stated	Target
	Patients were also instructed to collect saliva by themselves	Threshold		E gene
	Dry/direct sampling	As for reference index sample		Threshold
	Nasopharyngeal	Threshold predefined		A positive result was considered when the human RNase gene or the internal amplification control were positive and the cycle threshold (Ct) value was less than 40
	swab and saliva samples were transported at room temperature to the laboratory within 2 h of sample collection.	As for reference index sample		Threshold predefined
				Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Escobar 2021 127 (54)	Saliva not otherwise specified	Extraction As for reference index sample	Nasopharyngeal swab	RT-PCR
	Device Manufacturer Not stated	Testing method As for reference index sample	Operator Healthcare worker	Manufacturer TaqMan™ 2019-nCoV Assay Kit v1 (Applied Biosystems, CA, USA)
	Operator Patient/parent	Target As for reference index sample	Collection method Not stated	Extraction ExiPrep 96 Viral DNA/RNA Kit, ExiPrep™ 96 Lite (BIONEER, Daejeon, South Korea)
	Collection method The samples were obtained by self-sampling by the patient, who deposited a volume between 1 and 2 mL of saliva into a sterile nuclease-free 15 mL centrifuge tube. At least 30 min before sampling, each patient followed several specific guidelines: (1) no ingested food or liquids, except water; (2) no gum chewing; (3) no smoking or use of any type of mouth spray; and (4) no toothbrushing, no mouthwash, or dental floss. In addition, the participant had to remove cosmetic products, such as lip balms, and/or creams, when applicable.	Threshold As for reference index sample	Nasopharyngeal swab collected after saliva. No further details	Target N gene
	Dry/direct sampling	Threshold predefined As for reference index sample		Threshold Ct value < 37 or two replicates with Ct values of 38 were considered positive.
				Threshold predefined Yes
Felix 2022 50 (10)	Saliva spit	Extraction As for reference index sample	Nasopharyngeal swab	RT-PCR
	Device Manufacturer Not stated	Testing method As for reference index sample	Operator Not stated; presume healthcare worker	Manufacturer Altona RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Altona Diagnostics GmbH, Hamburg, Germany)
	Operator Patient/parent	Target As for reference index sample	Collection method Not stated	Extraction Viral RNA mini kit (Qia-gen, GE)
	Collection method Children were asked to spit into a sterile container for collection of about 1 mL of saliva.	Threshold As for reference index sample		Target S gene
		Threshold predefined As for reference index sample		Threshold Ct < 40 for positivity
				Threshold predefined Yes
Da Costa Fernandes 2021	(B) Saliva drool	Extraction MagaBio plus Virus DNA/RNA purifica-	Nasopharyngeal swab	RT-PCR
	Device Manufacturer Not stated	Operator		Manufacturer

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

(a) 226 (84) (no RNA extraction) (b) 92 (76) (RNA extraction)	Operator	tion kit II (BioFlux, Bioer, China)	Healthcare worker	Novel Coronavirus (2019-nCoV) RT-PCR Detection Kit (Shanghai Fosun Long March Medical Science)
	Supervised patient/parent			
	Collection method	Testing method	Collection method	Extraction
	Saliva was collected by just letting the mouth drop accumulated saliva into empty sterile sputum containers.	Novel Coronavirus (2019-nCoV) RT-PCR Detection Kit (Shanghai Fosun Long March Medical Science)	1 mL sample preservation fluid (Biogen, China)	MagaBio plus Virus DNA/RNA purification kit II (BioFlux, Bioer, China)
	(A) Saliva drool; no RNA extraction		Nasopharyngeal swab samples were collected with a sterile flocked swab placed in a sterile tube.	
	Device Manufacturer	Target		Target
	Not stated	N, E and ORF1ab		N, E and ORF1ab
	Operator	Threshold		Threshold
	Supervised patient/parent	Ct ≤ 6 was defined as positive		Ct ≤ 36 was defined as positive
	Collection method Saliva was collected by just letting the mouth drop accumulated saliva into empty sterile sputum containers.	Threshold pre-defined		Threshold pre-defined
		Yes		Yes
		Extraction		
		No RNA extraction (proteinase K (NZYTech, Portugal) and heating at 95 °C for 5 min		
		Testing method		
		Novel Coronavirus (2019-nCoV) RT-PCR Detection Kit (Shanghai Fosun Long March Medical Science)		
		Target		
		N, E and ORF1ab		
		Threshold		
		Ct ≤ 36 was defined as positive		
		Threshold pre-defined		
		Yes		
Fernandez-Gonzalez 2021(a); Fernandez-Gonzalez 2021(b);	Saliva spit, supervised	Extraction	Nasopharyngeal swabs	RT-PCR
	Device Manufacturer	As for reference index test	Operator	Manufacturer
	Collection pot			

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Fernandez-Gonzalez 2021 (c) [A 229 (50) - saliva supervised collection [B] 140 (27) - oropharyngeal washing [C] 208 (42) - saliva self-collection	Operator		Testing method	Healthcare worker (HCW)	LightMix Modular SARS-CoV (COVID19) E-gene kit; TIB Molbiol, Berlin, Germany; distributed by Roche
	Supervised patient		As for reference index test		
	Collection method		Target	Collection method	
	Subjects were instructed to produce and pool saliva in their mouths for 1 to 2 min, moving the mouth and passing the tip of the tongue across the cheeks and gums, and then to repeatedly spit a minimum of 1 mL saliva into the collection pot in the presence of a healthcare worker.		As for reference index test	3 mL of sterile transport medium containing guanidine salt (Mole Bioscience, SUNGO Europe B.V., Amsterdam, Netherlands)	Extraction
	100-mL sterile empty container without transport medium		Threshold		Chemagic 360 nucleic acid purification instrument (PerkinElmer España SL, Madrid, Spain)
	Samples were frozen (-20 °C)		As for reference index test	A flexible minitip swab was passed through the patient's nostril until the posterior nasopharynx was reached, left in place for several seconds to absorb secretions, and then slowly removed while rotating.	Target
	Saliva spit, unsupervised		Threshold predefined		E gene
	Device Manufacturer		As for reference index test		Threshold
	Collection pot		Extraction		CT value of ≤ 40
	Operator		As for reference index test		Threshold predefined
	Unsupervised patient		Testing method		Yes
	Collection method		As for reference index test		
	Saliva specimens were collected independently by the individual providing the sample, following written instructions.		Target		
	100-mL sterile empty container without transport medium		As for reference index test		
	Samples were frozen (-20 °C)		Threshold		
			As for reference index test		
			Threshold predefined		
			As for reference index test		
Fernández-Pittol 2020 51 (37)	Saliva deep throat		Extraction	Nasopharyngeal/oropharyngeal	MagNA Pure Compact Instrument (Roche, Basel, Switzerland);
	Device Manufacturer		As for reference index sample		
	(SARSTEDT, Germany).		Testing method	Operator	One step real time RT-PCR RNA Process Control Kit (Roche, Basel, Switzerland)
	Sample collection		As for reference index sample	Healthcare worker	
	Patient instructed and supervised by a healthcare worker		Target	Collection method	Targets
	Saliva sample provided from the posterior oropharynx before toothbrushing and meal intake. Participants were asked to collect saliva in their mouth and to gently spit it by aid of a funnel in a sterile cryotube collection tube. Saliva samples		As for reference index sample	Swab	E gene
			Threshold	Sample placed in 2 mL lysis buffer (guanidine thiocyanate, 2M; sodium citrate pH 7.0,	Threshold
			As for reference index sample		Not stated

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	with a volume less than 500 µL were not included in the study.	Threshold pre-defined	30 mM; dithiothreitol, 2 mM and triton X-100, 1%). The samples were transported to the Clinical Microbiology Department of the Hospital Clinic in Barcelona, Spain, within less than 2 hours after collection.	Threshold pre-defined
	Samples were transported to laboratory within 2 hours of collection. All saliva samples were stored at -80 °C and processed together.	As for reference index sample		Yes
FIND (a) 2021	Nasal anterior nares	Extraction	Nasopharyngeal swab	Antigen
218 (79)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	NowCheck COVID-19 Ag TestRG1901DGN (Nasal), Bionote, Inc.	Testing method	Not stated	NowCheck COVID-19 Ag Test; RG1901DG (nasopharyngeal)
	Operator	As for reference index sample	Collection method	Extraction
	Not stated	Target	Not stated	Not applicable
	Collection method	As for reference index sample		Target
	Test kit storage 2-30 °C	Threshold		Not stated
	No further details	As for reference index sample		Threshold
		Threshold pre-defined		Not stated
		As for reference index sample		Threshold pre-defined
				Yes
FIND (b) 2021	Nasal mid-turbinate	Extraction	Nasopharyngeal swab	Antigen
281 (22)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Panbio COVID-19 Ag Rapid Test Device Nasal (41FK11 (nasal version evaluated)	Testing method	Not stated	Panbio COVID-19 Ag Rapid Test Device Nasopharyngeal 41FK10 (nasopharyngeal evaluated)
	Operator	As for reference index sample	Collection method	Extraction
	Not stated	Target	Not stated	Not applicable
	Collection method	As for reference index sample		Target
	Test kit storage 2-30 °C	Threshold		Not stated
	No further details	As for reference index sample		Threshold
		Threshold pre-defined		Not stated
				Threshold pre-defined

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

		As for reference in- dex sample		Yes
FIND (c) 2021(a)	Nasal anterior nares	Extraction	Nasopharyngeal swab	Antigen
179 (42)	Device Manufacturer	As for reference in- dex sample	Operator	Manufacturer
	STANDARD Q COVID-19 Ag Test 09COV31D.SD Biosensor, Inc.	Testing method	Not stated	STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosen- sor, Inc.
	Operator	As for reference in- dex sample	Collection method	Extraction
	Not stated	Target	Kit extraction buffer	Not applicable
	Collection method	As for reference in- dex sample	Not stated	Target
	Not stated	Threshold		Not stated
	Kit extraction buffer	As for reference in- dex sample		Threshold
	2-30 °C	Threshold prede- fined		Not stated
		As for reference in- dex sample		Threshold prede- fined
				Yes
FIND(c) 2021 (b)	Nasal anterior nares	Extraction	Nasopharyngeal swab	Antigen
214 (78)	Device Manufacturer	As for reference in- dex sample	Operator	Manufacturer
	STANDARD Q COVID-19 Ag Test 09COV31D.SD Biosensor, Inc.	Testing method	Not stated	STANDARD Q COVID-19 Ag Test 09COV30D.SD Biosen- sor, Inc.
	Operator	As for reference in- dex sample	Collection method	Extraction
	Not stated	Target	Kit extraction buffer	Not applicable
	Collection method	As for reference in- dex sample	Not stated	Target
	Kit extraction buffer	Threshold		Not stated
	2-30 °C.	As for reference in- dex sample		Threshold
	No further details	Threshold prede- fined		Not stated
		As for reference in- dex sample		Threshold prede- fined
				Yes
FIND(s) 2021	Nasal not otherwise specified	Extraction	Nasopharyngeal swab	Antigen
369 (121)	Device Manufacturer	Not applicable	Operator	Manufacturer
	Sure Status® COVID-19 Antigen Card Test – Nasal Swab	Testing method	Not stated	Not stated
	Operator	Ag	Collection method	Extraction
	Not stated	Target		Not applicable

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Collection method	Not stated	Not stated	Target
	Not stated	Threshold		Not stated
	Test kit stored between 4 and 300 °C	Not stated		Threshold
		Threshold pre-defined		Not stated
		Yes		Threshold pre-defined
				Yes
Fougere 2021 397 (106)	Saliva drool	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	Not stated		Manufacturer
	Not stated	Testing method	Operator	In-house RT-PCR on the automated molecular diagnostic platform targeting the E gene or using the SARS-CoV-2 test of the Cobas 6800 instrument (Roche, Basel, Switzerland).
	Operator	As for reference index sample	Health care worker (HCW)	
	Patient or supervised patient/parent	Target	Collection method	
	Collection method	As for reference index sample	3 mL Viral Transport Medium	
	Collection of a significant amount of saliva and the drooling of at least 10 µL of saliva in a tube when possible	Threshold	Unclear	Extraction
		As for reference index sample		Not stated
		Threshold pre-defined		Target
		As for reference index sample		E gene
				Threshold
				The cycle threshold (cycle when the RT-PCR was positive, i.e., above the threshold of fluorescence) was provided automatically by the instruments by using the default parameter.
				Threshold pre-defined
				Yes
Fronza 2021 (a) 32 (15)	Saliva not otherwise specified	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample		Manufacturer
	Saliva collection kit (Comedical, Trento, Italy)	Testing method	Operator	Novel Coronavirus Real Time Multiplex RT-PCR Kit (Liferiver)
	Operator	As for reference index sample	Health care worker (HCW)	
	Unsupervised patient/parent	Target	Collection method	Extraction
	Collection method		Not stated	MagMAX Viral/Pathogen Nucle-

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Individuals collected the saliva autonomously after reading or watching the instructions linked with the kit (www.covidsaliva.it/). Inclusion in the study required not having eaten, drunk or smoked for at least 30 minutes prior to saliva collection. Saliva samples were fluidified with the addition of 1 mL DTT 6.5 mM in water.	As for reference index sample Threshold As for reference index sample Threshold predefined As for reference index sample	Unclear	ic Acid Isolation Kit (Thermofisher) Target RdRp gene Threshold Ct > 40 for positivity Threshold predefined Yes
Fronza 2021 (b) 193 (77)	Saliva not otherwise specified Device Manufacturer Saliva collection kit (Comedical, Trento, Italy) Operator Unsupervised patient/parent Collection method Individuals collected the saliva autonomously after reading or watching the instructions linked with the kit (www.covidsaliva.it/). Inclusion in the study required not having eaten, drunk or smoked for at least 30 minutes prior to saliva collection. Saliva samples were fluidified with the addition of 1 mL DTT 6.5 mM in water.	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold predefined As for reference index sample	Nasopharyngeal swab Operator Healthcare worker (HCW) Collection method Not stated	RT-PCR Manufacturer Novel Coronavirus Real Time Multiplex RT-PCR Kit (Liferiver) Extraction MagMAX Viral/Pathogen Nucleic Acid Isolation Kit (Thermofisher) Target RdRp gene Threshold Ct > 40 for positivity Threshold predefined Yes
Goncalves 2021 [A&B] [A] 157 (27) for the oral gingival swab group [B] 207 (85) for the saliva spit group	Oral (gingival fluid) Device Manufacturer A tube with Viral Transport Medium Operator Not stated Collection method A rayon-tipped swab was rubbed against both the maxillary and the mandibular gingiva. After rubbing both right and left sides, the swab was placed in a tube with 2 mL of Viral Transport Medium. Saliva spit Device Manufacturer	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample	Nasopharyngeal Operator Healthcare worker Collection method Viral Transport Medium Nasopharyngeal swab collection was performed by introducing a rayon-tipped swab into the nasal cavity, directing it upwards (towards the eyes), at an	RT-PCR Manufacturer SARS-CoV-2 (2019-nCoV) CDC qPCR Probe Assay (Integrated DNA Technologies, IA, USA) Extraction Maxwell®16 Viral Total Nucleic Acid Purification Kit (Promega) Target N1 and N2 genes Threshold

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	A sterile receptacle	Threshold pre-defined	angle of 30 ° to 45 ° in relation to the upper lip. The swab was rotated 10 times while in the nasopharyngeal cavity, and allowed to rest for 30 seconds prior to removal.	Both targets (N1 and N2) amplified with cycle threshold (Ct) ≤ 37
	Operator			Threshold pre-defined
	Unsupervised patients	As for reference index sample		Yes
	Collection method			
	Patients were asked to spit into a sterile recipient, producing at least 1 mL of saliva.			
	Dry/direct sample			
	Samples were kept refrigerated until further analysis.			
Griesemer 2021 (a) [A&B] 236 (12)	Nasal swab	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Tubes with molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)	Testing method	Unclear (probably healthcare worker)	CDC 2019 nCoV real-time reverse transcription-PCR (RT-PCR) diagnostic panel
	Operator	As for reference index sample	Collection method	Extraction
	Unclear (probably healthcare worker)	Target		BioMérieux easyMAG or EMAG (bioMérieux Inc, Durham, NC)
	Collection method	As for reference index sample		MagNA Pure 96 system (Roche Diagnostics, Indianapolis, IN)
	Collection of nasopharyngeal samples was by bilateral swabbing on flocked swabs with insertion to approximately one inch and gentle rotation for several seconds.	Threshold		Target
	Samples were introduced in tubes containing 1 mL molecular transport medium.	As for reference index sample		N1 gene
	Molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)	Threshold pre-defined		Threshold
	Saliva drool	As for reference index sample		Ct < 40 (www.fda.gov/media/134922/download)
	Device Manufacturer			Threshold pre-defined
	Not stated			Yes
	Operator			
	Supervised patient			
	Collection method			
	Patients were instructed to refrain from eating, drinking, chewing gum or tobacco, or smoking for 30 min prior to collection and to work up saliva in their mouth, not cough, and to drool or gently spit the saliva into the container. Collected in sterile 50 mL conical tubes			

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Direct sampling				
Griesemer 2021 (b) [A&B] 227 (93)	Nasal swab not otherwise specified	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Tubes with molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)	Testing method	Unclear (probably healthcare worker)	CDC 2019 nCoV real-time reverse transcription-PCR (RT-PCR) diagnostic panel
	Operator	As for reference index sample	Collection method	Extraction
	Unclear (probably healthcare worker)	Target		BioMérieux easyMAG or EMAG (bioMérieux Inc, Durham, NC)
	Collection method	As for reference index sample	Molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)	MagNA Pure 96 system (Roche Diagnostics, Indianapolis, IN)
	Collection of nasopharyngeal samples was by bilateral swabbing on flocked swabs with insertion to approximately one inch and gentle rotation for several seconds.	Threshold		Target
	Samples were introduced in tubes containing 1 mL molecular transport medium.	As for reference index sample		N1 gene
	Molecular transport medium (MTM; Longhorn Vaccines and Diagnostics, LLC, San Antonio, TX)	Threshold predefined	Flocked nasopharyngeal swabs were inserted in the nasopharyngeal cavity to approximately 1 inch and gently rotated for 10 to 15 s.	Threshold
	Saliva drool	As for reference index sample	Samples were introduced in tubes containing 1 mL molecular transport medium.	Ct < 40 (www.fda.gov/media/134922/download)
	Device Manufacturer			Threshold predefined
	Not stated			Yes
	Operator			
	Supervised patient			
	Collection method			
	Patients were instructed to refrain from eating, drinking, chewing gum or tobacco, or smoking for 30 min prior to collection and to work up saliva in their mouth, not cough, and to drool or gently spit the saliva into the container. Collected in sterile 50 mL conical tubes			
	Direct sampling			
Guclu 2020 (a) 15 (5)	Saliva not otherwise specified	Extraction	Nasopharyngeal/oropharyngeal	EZ1 (Qiagen, Germany)
	Device Manufacturer	As for reference sample	Operator	Device:
	Not stated	Targets	Healthcare worker	Genesis RT-PCR SARS-CoV-2 (Primer Design, UK) kit
	Sample collection	Not stated	Collection method	Targets
	Patient supervised by healthcare worker	Threshold		Not stated
	Saliva collected in a sterile dry container and participants were told to close the lid	As for reference sample		

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	of the container after placing the saliva in it.	Threshold pre-defined	Dacron-flocked swab inserted first into the posterior oropharynx and the posterior pharynx was swabbed for 2-3 seconds. Swab then inserted through the nostril with a rotation movement until the nasopharynx was reached and swab rotated gently for 2-3 seconds.	Threshold Ct < 45 Threshold pre-defined Yes
	Direct samples were delivered to the lab within one hour.	As for reference sample	2 mL viral transport medium (VTM); samples were delivered to the lab within one hour.	
Guclu 2020 (b) 49 (30)	Saliva not otherwise specified Device Manufacturer Not stated Sample collection Patient supervised by healthcare worker Saliva collected in a sterile dry container and participants were told to close the lid of the container after placing the saliva in it. Direct samples were delivered to the lab within one hour.	Extraction As for reference sample Targets Not stated Threshold As for reference sample Threshold pre-defined As for reference sample	Nasopharyngeal/oropharyngeal Operator Healthcare worker Collection method Dacron-flocked swab inserted first into the posterior oropharynx and the posterior pharynx was swabbed for 2-3 seconds. Swab then inserted through the nostril with a rotation movement until the nasopharynx was reached and swab rotated gently for 2-3 seconds. 3 mL viral transport medium (VTM); samples were delivered to the lab within one hour.	EZ1 (Qiagen, Germany) Device: Genesis RT-PCR SARS-CoV-2 (Primer Design, UK) kit Targets Not stated Threshold Ct < 45 Threshold pre-defined Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Guzman-Ortiz 2021 156 (23)	Saliva spit	Extraction	Mixed nasopharyngeal/oropharyngeal swabs	RT-PCR
	Device Manufacturer Where used, transport medium was Hanks' balanced salt solution without phenol red (Thermo Fisher Scientific, Waltham, MA, USA). Operator Patients/parents; no details provided Collection method Saliva was collected by the participants after being instructed to gently spit 5 times into a sterile 50 mL centrifuge tube; they were not instructed to cough out or try to enrich their samples with sputum. Dry/direct sampling or where saliva was viscous, balanced salt solution without phenol red was added.	As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold predefined Yes	Operator Healthcare worker Collection method Hanks' balanced salt solution without phenol red (Thermo Fisher Scientific, Waltham, MA, USA) Not stated	Manufacturer GeneFinder COVID-19 Plus RealAmp kit (ELITechGroup, Puteaux, France) Extraction QIAamp Viral RNA mini kit (QIAGEN, Hilden, Germany) Target RdRp, E and N genes Threshold A sample was considered positive if at least one of the RdRp, N or E genes were amplified with a Ct ≤ 40. Threshold predefined Yes
Hamilton 2021 128 (17)	Saliva spit	Extraction	Nasopharyngeal	RT-PCR
	Device Manufacturer OMNIgene OM-505 collection tubes (DNA Genotek) Operator Supervised patient Collection method Patients were guided through saliva sample collection using the OMNIgene saliva collection method. IGI's swab sample collection medium (resulting in a 1:1 dilution)	As for reference standard sample Testing method As for reference standard sample Target As for reference standard sample Threshold As for reference standard sample Threshold predefined As for reference standard sample	Operator Healthcare worker Collection method IGI's swab sample collection medium (resulting in a 1:1 dilution) Hospital's standard collection kit; no details provided	Manufacturer PCR method, no details provided Extraction Robotic sample plating and RNA extraction Target N gene Threshold Ct values < 38 Threshold predefined Yes
Herrera 2021 2107 (240)	Saliva not otherwise specified	Extraction	Nasopharyngeal swabs	RT-PCR
	Device Manufacturer 50 mL sterile conical centrifuge tube without preservatives	As for reference standard Testing method	Operator	Manufacturer US CDC realtime RT-qPCR protocol

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Operator	As for reference standard	Healthcare worker (HCW)	Extraction
	Patients; no more details			MagMAX Viral/Pathogen Nucleic Acid Isolation Kit (Thermo Fisher Scientific)
	Collection method	Target	Collection method	Target
	Saliva samples were self-collected by the individuals without any stimulation and without rinsing the mouth before sample collection.	As for reference standard	3 mL of Viral Transport Medium	N1 and N2 genes
		Threshold	Nasopharyngeal samples were collected using a flexible nylon swab that was inserted through the patient's nostrils to reach the posterior nasopharynx. It was left in place for several seconds and slowly removed while rotating.	Threshold
		As for reference standard		Ct value < 40
		Threshold predefined		Threshold predefined
		As for reference standard		Yes
Huber 2021 (a); Huber 2021 (b); Huber 2021 (c) 1270 (273)	Saliva spit:	Extraction	Nasopharyngeal swab	RT-PCR
	435/1270 (34%) enhanced spit (posterior oropharynx)	As for reference index sample	Operator	Manufacturer
	Device Manufacturer	Testing method	Healthcare worker-collected/laboratory staff-interpreted according to manufacturer's instructions	Cobas SARS-CoV-2 IVD test (Roche)
	One tube for saliva collection (Sarsted 105 62.555.001)	As for reference index sample		Extraction
	Operator	Target	Collection method	Nuclisens easyMAG Lysis Buffer (BioMérieux)
	Supervised patient-collected/laboratory staff-interpreted according to manufacturer's instructions	As for reference index sample		Target
	Collection method	Threshold	Universal Transport Medium or Viral Transport Medium: Cobas PCR Medium (Roche), Liquid amies preservation medium (Copan), Virus Preservative Medium (Improviral), or in-house Viral Transport Medium (HEPES, DMEM, FCS, antibiotics, antimycotics)	E and ORF1
	Saliva was collected directly after nasopharyngeal swab. Viral Transport Medium added to crude saliva	As for reference index sample		Threshold
	Study arm - Basic n = 835: individuals were asked to clear the throat thoroughly and collect saliva one or two times into the same tube	Threshold predefined		Ct values < 40
	Study arm - Enhanced N = 435: clear their throat three times thoroughly and collect saliva into the same tube. Emphasis was put on throat clearing to ascertain sampling material from the posterior oropharynx	As for reference index sample		Threshold predefined
	UTM or Viral Transport Medium		Saliva was collected directly after nasopharyngeal swab. Universal Transport Medium or	Yes (although re-testing of discordant using an in-house RT-qPCR for the E-gene with Corman's protocol)

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

			Viral Transport Medium swab according to manufacturer's instructions	
Justo 2021	Saliva not otherwise specified	Extraction	Nasopharyngeal swabs	RT-PCR
76 (41)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	A sterile tube	Testing method	Not stated	Multiplex RT-PCR commercial kit (GeneFinder, OSANG, South Korea)
	Operator	As for reference index sample	Collection method	Extraction
	Patient/parent	Target	Not stated	Quick-RNA Viral Kit (Zymo Research, Irvine, CA)
	Collection method	As for reference index sample		Target
	The participants were asked to self-collect 2 mL of their saliva in a sterile tube, avoiding mucous secretions from the oropharynx and sputum.	Threshold		RdRP, E and N genes
	Dry/direct sampling	Threshold predefined		Threshold
	As for reference index sample	Yes		A positive result was considered with a Ct value to lower than 40, for at least two SARS-CoV-2 genes (RdRp, E or N).
				Threshold predefined
				Yes
Kannian 2021	Saliva/whole mouth fluid	Extraction	Nasopharyngeal swabs	RT-PCR
80 (57)	Device Manufacturer	As for reference standard	Operator	Manufacturer
	Collected in sterile wide-mouthed screw-capped containers by drooling	Testing method	Not stated	In-house RT-PCR using commercial master-mixes (Taqman-based Labgenomics Labgun AssayPlus or Exofast, Siemens, Germany)
	Operator	As for reference standard	Collection method	Extraction
	Not stated	Target	3 mL of Viral Transport Medium	QIA Amp Viral RNA kit, Qiagen, Germany
	Collection method	As for reference standard	swab; no details provided	Target
	Not stated	Threshold		N and RdRP gene
		As for reference standard		Threshold
		Threshold predefined		A cycle threshold (Ct) value of less than 37.5 with AssayPlus or 27.5
		As for reference standard		

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

				with Exofast for one or two of the genes was considered positive.
				Threshold pre-defined
				Yes
Kerneis 2021 (a); Kerneis 2021 (b); Kerneis 2021 (c)	Saliva spit	Extraction	Nasopharyngeal	RT-PCR
1328 (112)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	50 mL tube	Testing method	Healthcare worker	TaqPath™ COVID 19 CE IVD RT PCR Kit (Thermo Fisher Scientific, Coutaboeuf, France)
	Operator	As for reference index sample	Collection method	Extraction
	Supervised patient	Target	Universal Transport Medium	MGEasy Nucleic Acid Extraction Kit (MGI Tech Co, Shenzhen, China)
	Collection method	As for reference index sample	sterile nylon flocked swab	Target
	Participants were asked to salivate in their mouth without clearing their throat and to repeatedly spit into a 50 mL tube up to a maximum of 3 mL.	Threshold		ORF1ab, N and S genes
	Dry/direct sampling	NAAT results were considered positive if at least one gene was detected: either N, S, or ORF1ab (for MGI-1 and MGI-2), and either E or ORF1ab (for Roche).		Threshold
	Samples were frozen in several aliquots at -80 °C within 24 hours and stored for analysis.	Threshold pre-defined		NAAT results were considered positive if at least one gene was detected: either N, S, or ORF1ab (for MGI-1 and MGI-2), and either E or ORF1ab (for Roche).
		Yes		Threshold pre-defined
				Yes
Klein 2021	Nasal mid-turbinate	Extraction	Nasopharyngeal swab	Antigen
290 (45)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	As for reference index sample	Testing method	Healthcare worker. Interpreted by trained study personnel following manufacturer's instructions	Panbio™ Ag-RDT (distributed by Abbott, Rapid Diagnostics, Jane, Germany)
	Operator	As for reference index sample	Order of collection and number of nostrils not clear	Extraction
	Supervised patient/parent took swab. Interpreted by trained study personnel following manufacturer's instructions. Order of collection and number of nostrils not clear	Target		Not applicable
	Collection method	As for reference index sample		Target
	Non-flocked swab ((Jiangsu	Threshold	Collection method	Not stated
				Threshold

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Changfeng Medical Industry Co., Ltd., Jiangsu, China) as part of the commercial RDT kit	As for reference index sample	Commercial kit not otherwise specified; flocked swab as part of commercial Ag kit (NFS-SWAB Applicator™, Noble Biosciences Inc., Gyeonggi-do, Korea)	The Panbio was conducted on-site by trained study personnel following the manufacturer's instruction for use for each kit.
		Threshold predefined		Threshold predefined
		As for reference index sample		Yes; according to manufacturer
Kocagoz 2021	Unconcentrated mouthwash - gargle	Extraction	Nasopharyngeal swab	RT-PCR
363 (114)	Device Manufacturer	No extraction	Operator	Manufacturer
	Not stated	Testing method	Healthcare worker. Laboratory-interpreted	Direct RT-PCR using commercial PCR kits (Bioeksan and A1 Lifesciences, Istanbul, Turkey)
	Operator	As for reference sample	Collection method	Extraction
	Patient-collected Laboratory-interpreted	Target	Not stated	No extraction
	Collection method	Not stated		Target
	After collecting nasopharyngeal swab samples, patients were instructed to take a few sips of regular drinking water, and then to gargle and rigorously rinse their mouth forcefully with this water for at least 10 s and put it back into an empty cup.	Threshold		Not stated
		Not stated		Threshold
		Threshold predefined		Not stated
		As for reference index sample		Threshold predefined
				Unclear. Assume yes as commercial kit used
Kojima 2020	(A) Nasal mid-turbinate	Extraction (A), (B) and (C)	Nasopharyngeal	RNA purification kit, Norgen Biotek Corp, Thorold, ON, Canada;
45 (29)	Device Manufacturer	As for reference sample	Operator	Healthcare worker
	CLASSIQSwabs, Copan Diagnostics, Murrieta, CA, USA + a tube with a ribonucleic acid storage media (DNA/RNA Shield solution, Zymo Research Corp, Irvine, CA, USA)	Targets	Collection method	RT-PCR single colour TaqMan probe modified by Integrated DNA Technologies, Coralville, IA, USA. Samples run on RT-PCR System (CFX 96™ Touch RT-PCR detection system or CFX 96™ Connect RT-PCR Detection System, Bio-Rad, Hercules, CA, USA)
	Sample collection	As for reference sample	Swab (Becton, Dickinson and Company, Franklin Lakes, NJ, USA)	
	Patient supervised by healthcare worker	Threshold		Targets
	Insert swab into one nostril to depth 3-4 cm, rotate swab for 5-10 seconds	As for reference sample	Samples transported to the laboratory at ambient temperature for testing on the day of collection.	N1 gene, N2 gene, N3
	Ribonucleic acid storage media Samples were transported to the laboratory at ambient temperature for testing on the day of collection.	Threshold predefined		
		As for reference sample		

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

(B) Saliva deep throat		Threshold		
Device Manufacturer		Not stated		
DNA/RNA Shield solution, Zymo Research Corp, Irvine, CA, USA		Threshold pre-defined		
Sample collection		Not stated		
Patient, supervised by healthcare worker				
Sterile swab not otherwise specified. Cough deeply 3-5 times, collect phlegm/secretions in mouth, rub swab on both cheeks, above and below tongue, both gums and hard palate for 20 seconds.				
As for sample (A) Nasal mid-turbinate				
(C) Saliva deep throat				
Device Manufacturer				
Testing kit: Sterile swab + a tube with a ribonucleic acid storage media (DNA/RNA Shield solution, Zymo Research Corp, Irvine, CA, USA)				
Sample collection				
Patient unsupervised				
Sterile swab not otherwise specified. Cough deeply 3-5 times, collect phlegm/secretions in mouth, rub swab on both cheeks, above and below tongue, both gums and hard palate for 20 seconds.				
Labhardt 2022 1986 (115)	Nasal anterior nares swab	Extraction	Nasopharyngeal swab	Antigen
	Device Manufacturer	Not applicable	Operator	Manufacturer
	As for reference index sample	Testing method	Healthcare worker-conducted and -interpreted	STANDARD Q COVID-19 Ag Test commercial test kits (SD Biosensor, Republic of Korea)
	Operator	As for reference index sample	Collection method	Extraction
	As for reference index sample	Target	Commercial kit not otherwise specified	Not applicable
	Collection method	As for reference index sample	Nasopharyngeal sample collection was done after nasal sampling by inserting the nasopharyngeal swab in horizontal position into the back of the nasopharynx un-	Target
	Prior to sample collection, participants had to blow their nose. Once the participant was seated, with their head back slightly, the swab was inserted while rotating it in each nostril, gently pushing the swab up to about 2 cm into the nostril until resistance was met and rotated for 3-5 seconds.	Threshold		Nucleocapsid antigen
		As for reference index sample		Threshold
		Threshold pre-defined		Visible line considered as positive
		As for reference index sample		Threshold pre-defined
				Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

				til resistance was felt, while rotating the swab at least 5 times.
Landry 2020 124 (35)	Saliva drool Device Manufacturer Not stated Operator Patient Collection method Provided with instructions to collect saliva from the deep throat (posterior oropharynx) Samples were kept in a cooler and delivered within 2 hours to the laboratory. Samples were frozen on day of receipt at -70 °C and thawed and tested 2 weeks later. Viscous saliva samples were liquefied by treating with sputasol (Thermo Scientific).	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold Not stated Threshold pre-defined As for reference index sample	Nasopharyngeal swab Operator Not stated Collection method Stored in 3 mL of universal transport medium (Becton Dickinson), cooled and delivered for processing on the day of collection. Residual +ve nasopharyngeal swab samples were frozen on day of receipt at -70 °C and thawed and tested 2 weeks later.	EasyMag (bioMerieux, Durham, NC); RT-PCR LDT developed assay based on CDC protocol Targets NN1 gene, N2 gene, RdRp Threshold Not stated Threshold pre-defined Yes Nasopharyngeal blind to saliva (drool) Unclear if saliva (drool) blind to nasopharyngeal
Leung 2020 62 (29) patients 95 (58) samples (analysis)	Saliva deep throat Manufacturer Not stated Operator Patient Sample Collection Provided with instructions to collect saliva from the deep throat (posterior oropharynx) Viral Transport Medium (2 mL) collected in a 'sterile sputum container'. Collected specimens were sent to laboratory immediately for testing.	Extraction As for reference sample Targets As for reference sample Threshold As for reference sample Threshold pre-defined As for reference sample	Nasopharyngeal Operator Healthcare worker Collection method Flocked swab Viral Transport Medium (3 mL) collected specimens sent to laboratory immediately for testing	Viral RNA isolation kit (Applied Biosystem, Foster City) + MagMAX kit; LightMix Modular SARS-CoV (COVID-19) E-gene detection kit (TIB Molbiol, Berlin, Germany). Test positives received additional different RT-PCR assay (not otherwise specified) Targets E gene and RdRp gene Threshold E gene and RdRp gene both positive Threshold pre-defined Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Lindner 2021 (b)	Nasal mid-turbinate	Extraction	Nasopharyngeal	Antigen
146 (40)	Device Manufacturer	Not applicable	Operator	Manufacturer
	Not stated	Testing method	Trained health-care worker-collected/trained healthcare worker-interpreted according to manufacturer's instructions	As for reference index sample
	Operator	Ag (CGIA) STANDARD Q COVID-19 Ag Test SD Biosensor, Inc. Gyeonggi-do, Korea; also distributed by Roche		Extraction
	Unsupervised patient-collected/unsupervised patient-interpreted according to manufacturer's instructions			Not applicable
	Collection method	Target	Collection method	Target
	Flocked swab. "Nasal swabs used for self-sampling less flexible with a larger sampling surface compared to nasopharyngeal swabs". Mirror and timer provided. Observed by healthcare worker but no intervention.	Not stated	Commercial kit not otherwise specified	Not stated
	1) "Cover your nose with a tissue and blow once"; 2) "Remove the swabs from the packaging by pulling on both flaps of the plastic film. Only touch the swab at the handle, not at the tip with the cotton";	Threshold	Collection: flexible flocked nasopharyngeal swab after nasal mid-turbinate swab collection. Professional test interpretation was by two study physicians, each blinded to the result of the other.	Threshold
	3) "Tilt your head back slightly (angle approx. 70 degrees)"; 4) "Insert the swab into a nostril with the cotton swab first. Slowly move the swab forward about 2 cm according to the angle (parallel to the palate = towards the throat, not upwards) until you feel resistance, do not apply pressure"; 5) "Slowly rotate the swab around for 15 seconds (minimum 4 rotations), rubbing all sides of the swab against the inside of the nose"; 6) "Repeat the procedure with the same swab in the other nostril".	The participant interpreted the test result as positive, negative, invalid, or 'don't know'		The visual read-out of the antigen test band was categorised as negative, weak positive, positive, or strong positive. Weak positives were classified as positive.
	Interpretation:	Threshold predefined		Threshold predefined
	1) "Open the extraction buffer tube and insert the swab with the cotton part first";	Yes		Yes
	2) "While squeezing the buffer tube in the lower part, stir the swab more than 10 times"; 3) "Remove the swab while squeezing the sides of the tube in the lower part to extract the liquid from the swab"; 4) "Press the nozzle cap tightly onto the tube"; 5) "Open the foil pouch of the test card at the tear line and put the test device on the table"; 6) "Place the test horizontally in front of you"; 7) "Hold the tube vertically over the marked round field (not the rectangle result window)"; 8) "Squeeze the tube for applying 4 drops of extracted specimen to the specimen well of the test device". After 15 minutes, the participant was asked to state his/her interpretation			

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

of the test result (positive, negative, invalid, or don't know).
"The participants received written and illustrated instructions in German or English, adapted from the manufacturer's instructions for use".

Lopes 2021 [A&B] Nasopharyngeal vs Oropharyngeal: 1440 (267) Nasopharyngeal vs Saliva: 1440 (295) Nasopharyngeal vs Saliva Viral Transport Medium: 1440 (280)	Saliva spit [A]	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer Sterile sputum containers containing 300 uL of 0.9% NaCl solution Operator Supervised patient Collection method Patients were requested to avoid eating, drinking, and smoking for at least 30 min prior to spit into the sterile tube containing saline solution (0.9% NaCl). Specimens were considered acceptable if at least 1 mL of saliva has been obtained. Saline solution. As for reference index sample Oropharyngeal swab [B] Device Manufacturer 5 mL tube Operator Healthcare workers Collection method For the collection of the oropharyngeal swab, the swab was inserted in the oral cavity, then rubbed on the posterior part of the pharynx and regions of the tonsils, avoiding contact with the tongue, teeth, and gums. 3 mL viral transport medium (VTM)	As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold predefined Yes	Operator Healthcare worker Collection method 3 mL viral transport medium (VTM) Nasopharyngeal swab collection was performed by rubbing a swab on the posterior part of the nostril, with a rotation movement until the nasopharynx was reached, and the sample was obtained by rotating the swab gently for 5 s.	Manufacturer Molecular kit SARS-CoV-2 (E) (Bio-Manguinhos/Fiocruz, Rio de Janeiro, Brazil) Extraction Automatic MDX Biorobot® (Qiagen, Hilden, Germany) Target RdRp and E genes Threshold Ct values < 40 were considered positive Threshold predefined Yes
Mahmoud 2021 595 (250)	Saliva spit	Extraction	Nasopharyngeal	RT-PCR
	Device Manufacturer Sterile Dnase/ Rnase-free container Operator Patient; no details provided Collection method	No RNA extraction Testing method As for reference index sample Target As for reference index sample	Operator Healthcare worker Collection method Viral Transport Medium	Manufacturer BGI Genomics' 2019-nCoV Fluorescence Detection Real-Time RT-PCR kit Extraction Not stated; "RNA extraction was per-

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Participants were asked to pool saliva in his or her mouth for 1–2 minutes before depositing the salivary sample into a collection tube. Dry/direct sampling Salivary samples were transported to the lab in temperature-controlled boxes at 2-8 degrees Celsius.	Threshold As for reference index sample Threshold predefined As for reference index sample	formed by the automated machine MGISP-960, as per the manufacturer's instructions" Target ORF1ab Threshold Ct values < 38 Threshold predefined Samples with CT values > 38 and S-shaped amplification curves are considered in the grey zone and were re-processed for confirmation.
Marquette 2021 (a); Marquette 2021 (b); Marquette 2021 (c) [1] 409 (116) [2] 147 (59) [3] 262 (57)	Saliva salivate Device Manufacturer Small hydroxylated polyvinyl acetate (PVA) sponges (Merocel® Standard Dressing, réf 400400, Medtronic) Operator Not stated; assume healthcare worker Collection method Mall hydroxylated poly vinyl acetate (PVA) sponges placed in mouth by participants and taken out after one minute and inserted into a sterile collection tube. No instructions were given regarding the need to fast, to have chewed gum or smoked a cigarette/e-cigarette. "After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: Nasopharyngeal and OS in a random order".	Extraction Viral RNA extraction buffer (RNA/DNA purification kit, DaAn Gene, ref DA0940) Testing method -Symptomatics: DaAnGene DA0992-Detection Kit for 2019-nCoV (DaAn Gene Co., Ltd. Sun Yat-sen University, Guangzhou, Guangdong, China) -Close contacts: Idylla SARS-CoV-2 test cartridges (Bio-cartis) Target -Symptomatics: N, ORF1ab gene -Close contacts: N, ORF1ab gene Threshold -Symptomatics: Ct < 36 for positivity -Close contacts: a positive result required at least 2	Nasopharyngeal swab Operator Patient/parent Collection method Viral transport medium Samples were eluted into a vial "After signing an informed consent to participate, all volunteers were interviewed and underwent paired sampling: Nasopharyngeal and Oropharyngeal in a random order". RT-PCR Manufacturer -Symptomatics: DaAn-Gene DA0992-Detection Kit for 2019-nCoV (DaAn Gene Co., Ltd. Sun Yat-sen University, Guangzhou, Guangdong, China) -Close contacts: Aptima SARS-CoV-2 assay (Hologic, Inc. 10210 Genetic Center Drive San Diego, CA 92121 USA) Extraction -Symptomatics: Viral RNA extraction buffer (RNA/DNA purification kit, DaAn Gene, ref DA0940) -Close contacts: no RNA extraction (TMA technique) Target -Symptomatics: N, ORF1ab gene -Close contacts: ORF1ab gene Threshold

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

		amplified N targets [by setting a quantification cycle (Cq) of 41.9] and/or at least one or more amplified Orf1b targets		-Symptomatics: Ct < 36 for positivity -Close contacts: RLU above 850
		Threshold pre-defined		Threshold pre-defined
		As for reference index sample		Yes
Marx 2021 (a); Marx 2021 (b); Marx 2021 (c); Marx 2021 (d); Marx 2021 (e); Marx 2021 (f)[A&B]	Saliva swab Device Manufacturer Not stated Operator Supervised patient collection/healthcare worker-interpreted Collection method Not stated (specimens were collected according to current CDC guidelines) Not stated CDC Guideline states no Viral Transport Medium Nasal anterior nares swab Device Manufacturer Not stated Operator Supervised patient collection/healthcare worker-interpreted Collection method Not stated (specimens were collected according to current CDC guidelines) Not stated CDC Guideline states Viral Transport Medium	Extraction Marx 2021 (f)(A) & (B) Not stated Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined As for reference index sample	Nasopharyngeal swab Operator Healthcare worker-collected/healthcare worker-interpreted Collection method Not stated (specimens were collected according to current CDC guidelines). CDC guideline stated Viral Transport Medium.	RT-PCR Manufacturer CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay Extraction Not stated Target N1, N2 gene Threshold Ct < 40 for positivity Threshold pre-defined Yes
Marx 2021 (g); Marx 2021 (h); Marx 2021 (i); Marx 2021 (j); Marx 2021 (k); Marx 2021 (l); Marx 2021 (m); Marx 2021 (n); Marx 2021 (o); Marx 2021 (p); Marx 2021 (q);	Saliva swab Device Manufacturer Not stated Operator Supervised patient collection/healthcare worker interpreted Collection method	Extraction Marx 2021 (r)(A) & (B) Not stated Testing method As for reference index sample Target	Nasopharyngeal swab Operator Healthcare worker-collected/healthcare worker-interpreted	RT-PCR Manufacturer CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel assay Extraction Not stated

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Marx 2021 (r) [A&B]	Not stated (specimens were collected according to current CDC guidelines)	As for reference index sample	Collection method	Target N1, N2 gene
Nasal: 932 (74) Saliva: 864 (69)	Not stated CDC Guideline states no Viral Transport Medium Nasal anterior nares swab	Threshold As for reference index sample	Not stated CDC Guideline stated Viral Transport Medium.	Threshold Ct < 40 for positivity
	Device Manufacturer Not stated	Threshold predefined As for reference index sample	Not stated (specimens were collected according to current CDC guidelines)	Threshold predefined Yes
	Operator Supervised patient collection/healthcare worker-interpreted			
	Collection method Not stated (specimens were collected according to current CDC guidelines) Not stated CDC Guideline states Viral Transport Medium			
Matic 2020 74 (22)	Saliva spit Device Manufacturer Sterile screw-top container (Starplex Scientific Inc., Etobicoke, Canada) Operator Unsupervised patient Collection method Patients were asked to provide approximately 1 mL of saliva by pooling saliva in the mouth and spitting into a sterile screw-top container. Dry/direct sampling Saliva samples were transported to the laboratory at room temperature without the addition of transport media. In the laboratory, samples were diluted 1:2 with sterile phosphate-buffered saline.	Extraction As for reference index sample Testing method LightMix® ModularDx SARS-CoV (COVID19) E-gene assay (TIB Molbiol, Germany) Target E gene Threshold As for reference index sample Threshold predefined As for reference index sample	Nasopharyngeal swab Operator Healthcare worker Collection method 2 mL of Universal Transport Medium™ (COPAN, Brescia, Italy) or 3 mL of BD™ Universal Viral Transport System (Becton Dickinson, Sparks, MD); swabs were collected using COPAN Flocked Swabs.	Manufacturer LightMix® ModularDx SARS-CoV (COVID19) E-gene assay (TIB Molbiol, Germany) or the cobas® SARS-CoV-2 Test (Roche Molecular Diagnostics, Laval, QC) Extraction MagNA Pure 96 System (Roche Molecular Diagnostics, CA, USA) Target E gene and not stated Threshold Not stated Threshold predefined Yes
McCormick-Baw 2020 156 (50)	Saliva spit Device Manufacturer Not stated Sample collection	Extraction As for reference sample Targets	Nasopharyngeal Operator Not stated Collection method	RT-PCR Manufacturer Cepheid Xpert Xpress SARS-CoV-2 PCR test (Sunnyvale, CA)

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Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Healthcare worker trained to ensure saliva, not sputum collection	As for reference sample	Testing was performed according to the "manufacturer's instructions"	Targets E gene, N2 gene
	Unpreserved saliva samples (5 mL) were collected in sterile urine cups or sterile 50 mL conical tubes.	Threshold As for reference sample	Universal Transport Medium (5 mL). Specimens processed "on demand"	Threshold Detection of E gene and N2 gene, OR N2 gene alone
	"Once specimens were collected, they were labelled with a demographic label, double-bagged and submitted to the laboratory through the pneumatic tube system".	Threshold pre-defined As for reference sample		Threshold pre-defined Yes
	'Saliva samples were held at 2-8 °C for up to 12 hours prior to testing'.			
McCulloch 2020	Nasal mid-turbinate	Extraction As for reference sample	Nasopharyngeal	Roche Magna Pure 96, Viral NA small volume kit; one step RT-PCR. AgPath-ID system master mix on the real-time ABI 7500 instrument. Developed in-house.
158 (18) indeterminate classified +ve	Device Manufacturer Flocked mid-nasal swab (Copan Flo-qSwab 56380CS01, Copan Diagnostics, Murrieta, CA)	Targets As for reference sample	Operator Healthcare worker	
158 (14) indeterminate classified -ve	Sample collection	Threshold As for reference sample	Collection method Swab no further details	Targets N1 gene, N2 gene
	Patient provided with written instructions	Threshold pre-defined As for reference sample		Threshold Both N-gene targets: positive; one N gene: inconclusive result
	Flocked mid-nasal swab. No further details.			Threshold pre-defined Yes
	Universal Transport Media (UTM) (Becton Dickinson, Franklin, NJ)			
McLennan 2022	Saliva spit	Extraction As for reference index sample	Mixed Nasopharyngeal/oropharyngeal	RT-PCR
109 (11)	Device Manufacturer Universal specimen container	Testing method ABI TaqPath™ COVID-19 Multiplex Assay	Operator Healthcare worker	Manufacturer ThermoFisher
	Operator Unsupervised patient. A written information leaflet was provided to each eligible attendee and verbal consent for involvement was obtained prior to participation in the study.	Target As for reference index sample	Collection method Taken before saliva and gargle samples. No further details	Extraction Omega Biotek MAG-BIND® VIRAL DNA/RNA kit
	Collection method Those who agreed to take part were asked to produce a saliva sample by repeatedly pooling saliva in their mouth and spitting into a universal specimen container.	Threshold As for reference index sample		Target N, ORF and S genes
	Dry/direct sampling. Samples treated with proteinase K	Threshold pre-defined As for reference index sample		Threshold Not stated
				Threshold pre-defined Not stated

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Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

Specimens were transported to the lab by cold chain in coolboxes with ice packs. During Phase 1b participants were asked to produce 2 saliva samples (2 mL saliva per container), one stored and transported in a 4 °C refrigerator, and the other at ambient temperature.

Melo Costa 2021 (a); Melo Costa 2021 (b); Melo Costa 2021 (c) MIXED symptoms and asymptomatic: 273 (46) Asymptomatic: 183 (17) Symptomatic: 90 (29)	Saliva salivate Device Manufacturer Cotton roll (Neutral Salivettes®, SARST-EDT, Numbrecht, Germany) Operator Patient supervised by laboratory technician Collection method Each participant should not have eaten or drunk anything in the 30 minutes prior to saliva collection. Collected with a cotton roll (Neutral Salivettes®, SARST-EDT, Numbrecht, Germany) directly introduced in the mouth without handling and then kept for 2 min in the participant's mouth who soaked the cotton by doing circular movements, prior to replacing it in the stopper part of the Salivette® tube Dry sampling. Ultra-pure water was used if necessary to increase the volume of the sample.	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold predefined As for reference index sample	Nasopharyngeal swab Operator Not stated Collection method Viral Transport Medium Collected with nasal swabs with Viral Transport Medium following manufacturer's protocol	RT-PCR Manufacturer Protocol not stated; performed in a Light-Cycler 480II instrument (Roche Diagnostics®, Mannheim, Germany) Extraction NucleoMag® Pathogen Isolation kit (MACHERY NAGEL GmbH & Co, Düren, Germany) using the KingFisher™ Flex system (ThermoFisher Scientific, Villebon Courtaboeuf, France) Target E gene Threshold Ct value < 35 as positivity Threshold predefined Yes
	Saliva spit Device Manufacturer 'Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada Operator Supervised patient-collected/laboratory staff-interpreted Collection method Patients were asked not to eat, drink, smoke or use chewing gum in the last 30 minutes. Collection was made according to manufacturer's instructions.	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample	Nasopharyngeal swab Operator Healthcare worker or trained non-healthcare worker-collected/laboratory staff-interpreted Collection method Samples were collected in a transport buffer that	RT-PCR Manufacturer Taq one-step RT-qPCR mastermix (Bio-Rad, Temse, Belgium) Extraction Total RNA Purification Kit (Norgen Biotek #24300) according to the Manufacturer's instructions Target E, ORF1ab, N, S Threshold

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Samples were collected in a transport buffer that inactivates the virus and stabilises the RNA (DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA) Saliva swab/salivate Device Manufacturer Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada Operator Supervised patient-collected/laboratory staff-interpreted Collection method Patients were asked not to eat, drink, smoke or use chewing gum in the last 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to manufacturer's instructions. Samples were collected in a transport buffer that inactivates the virus and stabilises the RNA (DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)	Threshold pre-defined Yes	inactivates the virus and stabilises the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA) Patients were asked not to eat, drink, smoke or use chewing gum in the last 30 minutes. Collection was made according to the manufacturer's instructions.	2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37 (www.fda.gov/media/136112/download) Threshold pre-defined Yes
Mestdagh 2021 (d)[A]; Mestdagh 2021 (d)[B]; Mestdagh 2021 (e)[A]; Mestdagh 2021 (e)[B]; Mestdagh 2021 (f)[A]; Mestdagh 2021 (f)[B] 2491 (72)	Saliva spit Device Manufacturer Saliva RNA Collection and Preservation Device; Norgen Biotek, Thorold, ON, Canada Operator Supervised patient-collected/laboratory staff-interpreted Collection method Patients were asked not to eat, drink, smoke or use chewing gum in the last 30 minutes. Collection was made according to manufacturer's instructions. Samples were collected in a transport buffer that inactivates the virus and stabilises the RNA (DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA) Saliva swab/salivate	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined Yes	Nasopharyngeal swab Operator Healthcare worker or trained non-healthcare worker-collected/laboratory staff-interpreted Collection method Samples were collected in a transport buffer that inactivates the virus and stabilises the RNA (Norgen Biotek or DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer	RT-PCR Manufacturer TaqPath COVID-19 Combo Kit (Applied Biosystems) Extraction Magnetic bead-based RNA extraction method developed by University of Liège (CoRNA kit) according to the recommended protocol Target E, ORF1ab, N, S Threshold 2 or more SARS-CoV-2 gene targets with cycle threshold values of ≤ 37

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Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Device Manufacturer Oracollect RNA, DNA Genotek, Kanata, Ontario, Canada Operator Supervised patient-collected/laboratory staff-interpreted Collection method Patients were asked not to eat, drink, smoke or use chewing gum in the last 30 minutes. Participants were also instructed to place the swab between the right cheek and gum, swab 10 times, and repeat for the left cheek. Collection was made according to manufacturer's instructions. Samples were collected in a transport buffer that inactivates the virus and stabilises the RNA (DNA Genotek buffer for the respective saliva samples and 2 mL of DNA/RNA shield buffer, Zymo Research, Irvine, CA)	Zymo Research, Irvine, CA) Patients were asked not to eat, drink, smoke or use chewing gum in the last 30 minutes. Collection was made according to the manufacturer's instructions.	(www.fda.gov/media/136112/download) Threshold predefined Yes
Migueres 2020 123 (44)	Saliva drool Device Manufacturer Not stated Operator Patient Collection method Patients asked to salivate, swill the saliva around their mouth for at least 30 s and then spit into a sterile container.	Extraction As for reference sample Testing method As for reference index sample Targets As for reference sample Threshold Not stated Threshold predefined As for reference sample	Nasopharyngeal Operator Not stated Collection method Not stated RT-PCR (Hologic, Panther Fusion) Targets RdRp (IP2, IP4, Institut Pasteur, Paris, France) Threshold Not stated Threshold predefined Yes
Migueres 2021 (a); Migueres 2021 (b); Migueres 2021 (c) 301 (56)	Saliva spit Device Manufacturer Not stated Operator Supervised patient/supervised parent Collection method	Extraction Not stated Testing method As for reference index sample Target	Nasopharyngeal swab Operator Healthcare worker Collection method Laboratory-developed test (LDT) based on real-time RT-PCR on a Panther Fusion module (Hologic, San Diego, California) Extraction

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Saliva (1 mL) was collected after the participants had swilled their saliva around their mouths for at least 30 seconds and then spat into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM)	As for reference index sample	Viral Transport Medium (VTM)	Aptima lysis tube
		Threshold	Nasopharyngeal swabs were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM)	Target
		As for reference index sample		ORF1ab gene RdRp gene
		Threshold predefined		Threshold
		As for reference index sample		Ct > 35 for positivity
				Threshold predefined
				Yes
Migueres 2021 (d); Migueres 2021 (e); Migueres 2021 (f) 301 (55)	Saliva spit	Extraction	Nasopharyngeal swab	TMA
	Device Manufacturer	Not stated	Operator	Manufacturer
	Not stated	Testing method	Healthcare worker (HCW)	Aptima SARS-CoV-2 transcription-mediated amplification assay (TMA) (Hologic, San Diego, California)
	Operator	As for reference index sample	Collection method	Extraction
	Supervised patient/supervised parent	Target		Aptima lysis tube
	Collection method	As for reference index sample	Viral Transport Medium (VTM)	Target
	Saliva (1 mL) was collected after the participants had swilled their saliva around their mouths for at least 30 seconds and then spat into a sterile container. The saliva samples were diluted 3-fold in Minimum Essential Media (MEM)	Threshold	Nasopharyngeal swabs	ORF1ab gene RdRp gene
		As for reference index sample	were collected on flocked swabs and placed in 3.5 mL of virus transport medium (VTM).	Threshold
		Threshold predefined		Ct > 35 for positivity
		As for reference index sample		Threshold predefined
				Yes
Miller 2020 91 (36)	Saliva spit	Extraction	Nasopharyngeal	Manual method using the MagMAX Viral/Pathogen Nucleic Acid Isolation kit (ThermoFisher Scientific);
	Device Manufacturer	Not stated	Operator	COVID-19 RT-PCR test (new test, Phosphorus Diagnostics, LLC)
	Orasure Oragene DX (OGD-510) Device	Testing method	Healthcare worker	Targets
	Operator	As for reference index sample	Collection method	N1 gene, N2 gene, RdRp gene
	Patient-supervised	Target	Swab	Threshold
	Collection method	As for reference index sample	Viral Transport Medium. Samples were transported at ambient temperature and tested within 48 hr of collection.	Both N-gene targets: positive; one N gene: inconclusive result; Ct
	Saliva, collected 'according to Manufacturer's instructions'	Threshold		
	"Paired samples were transported at ambient temperature and tested within 48 hrs after collection"	As for reference index sample		
		Threshold predefined		

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

		As for reference in- dex sample		Threshold prede- fined
				Yes
Mora-Aguilera 2022 (a) 23 (9)	Sterile water gargle	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	Manual RNA extrac- tion: hot acid phe- nol method and CTAB	Operator	Manufacturer
	Screw-cap plastic bottle		Not stated (prob- ably healthcare worker)	Not stated; quote: "The Nasopharyngeal swab specimens, col- lected on cohorts 2 and 3, were submit- ted to a blind national reference laboratory to perform the official test accepted by the World Health Organi- zation (WHO)".
	Operator	Testing method	Collection method	
	Unsupervised patient	In-house RT-PCR protocol	Not stated	
	Collection method	Target		Extraction
	MWS was vigorously stimulated with 1 mL of sterile distilled water for 40 s. Individu- als were asked to avoid food eating and/ or toothbrushing at least 1 h before sam- pling, keep the mouth closed during the MWS procedure to avoid aerosols [13–15], and stick the ID label and close the lid af- ter collecting the total mouth fluids in a 100 mL sterile leak-proof, screw-cap plas- tic bottle containing 2 mL of lab-prepared viral Hanks's transport medium.	N and RPP30 genes		Not stated
		Threshold		Target
		Not stated		Not stated; quote: "The Nasopharyngeal swab specimens, col- lected on cohorts 2 and 3, were submit- ted to a blind national reference laboratory to perform the official test accepted by the World Health Organi- zation (WHO)".
		Threshold prede- fined		Threshold
		Not stated		Not stated
	2 mL of lab-prepared viral Hanks's trans- port medium			Threshold prede- fined
	Samples were stored at 4 °C/24 h.			Not stated
Mora-Aguilera 2022 (b) 22 (4)	Sterile water gargle	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	Manual RNA extrac- tion: hot acid phe- nol method and CTAB	Operator	Manufacturer
	Screw-cap plastic bottle		Not stated (prob- ably healthcare worker)	Not stated; quote: "The Nasopharyngeal swab specimens, col- lected on cohorts 2 and 3, were submit- ted to a blind national reference laboratory to perform the official test accepted by the World Health Organi- zation (WHO)".
	Operator	Testing method	Collection method	
	Unsupervised patient	In-house RT-PCR protocol	Not stated	
	Collection method	Target		
	MWS was vigorously stimulated with 1 mL of sterile distilled water for 40 s. Individu- als were asked to avoid food eating and/ or toothbrushing at least 1 h before sam-	N and RPP30 genes		

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Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	pling, keep the mouth closed during the MWS procedure to avoid aerosols [13–15], and stick the ID label and close the lid after collecting the total mouth fluids in a 100 mL sterile leak-proof, screw-cap plastic bottle containing 2 mL of lab-prepared viral Hanks's transport medium. 2 mL of lab-prepared viral Hanks's transport medium Samples were stored at 4 °C/24 h.	Threshold Not stated Threshold pre-defined Not stated	Extraction Not stated Target Not stated; quote: "The Nasopharyngeal swab specimens, collected on cohorts 2 and 3, were submitted to a blind national reference laboratory to perform the official test accepted by the World Health Organization (WHO)". Threshold Not stated Threshold pre-defined Not stated
Moreno-Contreras 2020 71 (34)	Saliva spit Device Manufacturer Sterile urine cup container; no manufacturer's name mentioned Operator Patient Collection method Saliva collected by repeatedly spitting into collection cup and mixed with lysis buffer No viral transport medium was added to the saliva samples. All samples were stored and kept at 4 °C until transported for analysis, which was within 24–36 hours after sample collection.	Extraction Quick Extract DNA Extraction Solution (QE, Lucigen) StarQ One-step RT-qPCR (Genes 2 Life) kit Testing method As for reference sample Targets Berlin Protocol: E gene and Rnase P Threshold Ct value ≤ 38 Threshold pre-defined As for reference sample	Nasopharyngeal/oropharyngeal Operator Healthcare worker Collection method Swab 2.5 mL Viral Transport Medium. Samples stored at 4 °C and transported for analysis within 24–36 hours after collection. Targets Berlin Protocol: E gene, RdRp Threshold Ct ≤ 38 Threshold pre-defined Yes
Nacher 2021 (a); Nacher 2021 (b) 1028 (223)	Saliva spit Device Manufacturer Urine container; no details provided Operator	Extraction As for reference sample Testing method	Nasopharyngeal swab Operator Healthcare workers Manufacturer GeneFinder COVID-19 Plus RealAmp

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Unsupervised patient	As for reference sample	Collection method	kit (ELITechGroup, Puteaux, France)
	Collection method	Target	"Transport Medium" not otherwise specified	Extraction
	Patients were advised not to eat or drink and to rinse their mouth before the test. Also to accumulate saliva in their mouth before spitting it in the dedicated container	As for reference sample	No further details	Qiasymphony system (QIAGEN, Hilden, Germany)
	Dry/direct sampling When saliva specimens presented high viscosity, they were fluidified with proteinase K using a 10% equivalent volume of the specimen, then vortexed and incubated at 56 °C during 15 minutes. If the collected volume of saliva was insufficient (< 1 mL), we completed up to 1 mL with NaCl 0.9% (192 samples (18.7%) were diluted with normal saline).	Threshold		Target
		As for reference sample		RdRp, E and N genes
		Threshold predefined		Threshold
		Yes		A sample was considered positive if at least one of the RdRp, N or E genes were amplified with a Ct < 40
				Threshold predefined
				Yes
Otto 2020	Saliva deep throat	Extraction	Nasopharyngeal	MagNA pure compact (Roche, Switzerland) or GenoExtract (Biocentric, France);
92 (49)	Device Manufacturer	As for reference sample	Operator	
	Not stated	Testing method	Healthcare worker	RT-PCR; in-house (French National Center) protocol using a Light-Cycler 480 Real-Time PCR System (Roche, Switzerland)
	Operator	As for reference sample	Collection method	
	Patient	Target	Viral Transport Medium Immediately transferred to laboratory and inactivated with 10 µL of proteinase K (25 mg/mL) into 200 µL of specimen at 65 °C over 10 minutes	Targets
	Collection method	As for reference sample		RdRp gene (IP2 and IP4 regions)
	Cough keeping surgical mask on, and then collect saliva in a sterile container	Threshold		Threshold
	No viral transport medium used; immediately transferred to laboratory and inactivated with 10 µL of proteinase K (25 mg/mL) into 200 µL of specimen at 65 °C during 10 minutes	As for reference sample		Not stated
		Threshold predefined		Threshold predefined
		Yes		Yes
Pasomsub 2020	Saliva spit	Extraction	Nasopharyngeal/oropharyngeal	MagDEA® Dx reagents (Precision System Science, Chiba, Japan);
200 (21)	Device Manufacturer	As for reference sample	Operator	
	Sputum collection container containing the Universal Transport Medium	Testing method	Not stated	Diagnostic Kit (Sansure, Changsha, China)
	Operator	As for reference sample	Collection method	Targets
	Not stated	Target		ORF1ab gene, N genes
	Collection method			

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

	Not stated	As for reference sample	Sterile Tube containing Copan's Universal Transport Medium	Threshold Ct both target genes $\leq$ 38. Retesting of samples with discordant gene Ct values. Specimens repeatedly discordant reported as negative
		Threshold		
	As for reference sample	As for reference sample	Collection	
		Threshold predefined	COPAN FLO-QSwabs	
	Yes		Copan's Universal Transport Medium. Viral RNA extracted from samples within 26 minutes of collection	Threshold predefined Yes
Patel 2020	Oropharyngeal	Extraction	Nasopharyngeal	RT-PCR
146 (25)	Device Manufacturer	As for reference sample	Operator	Manufacturer
	Not stated		Not stated	
	Operator	Testing method	Collection method	
	Not stated	As for reference sample	Swab. No further details	CDC 2019–Novel Coronavirus (nCoV) Real-Time Reverse Transcriptase (RT)-Polymerase Chain Reaction (PCR) Diagnostic Panel
	Collection method	Target		Targets
	Swab; no further details	As for reference sample		N1 gene, N2 gene, N3 gene
		Threshold		Threshold
		As for reference sample		Ct < 40 for all three gene regions
		Threshold predefined		Threshold predefined
		As for reference sample		Yes
Patriquin 2022	Oropharyngeal/nasal anterior nares swab	Extraction	Nasopharyngeal swab	RT-PCR
392 (64)	Device Manufacturer	As for reference sample	Operator	Manufacturer
	LASSIQSwab fiber-tip swab from Copan Italia (Brescia, Italy)	Testing method	Not stated. Probably healthcare worker	Samples were initially tested by the Aptima SARS-CoV-2 Assay on the Panther System (Hologic Inc., San Diego, CA); negative results were confirmed by the Cobas 6800 instrument (Roche Diagnostics, Rotkreuz, 74 Switzerland) and positive results by both the Roche 6800 assay
	Operator	As for reference sample	Collection method	
	Not stated. Probably healthcare worker	Target	Viral Transport Medium	
	Collection method	As for reference sample		
	According to a "previously described" collection technique. Collected after nasopharyngeal swab	Threshold	Standardised sampling technique with a flocked swab	
	Viral transport medium	As for reference sample		

Table 7. Study characteristics: details of testing (index and reference samples) (a) *(Continued)*

		Threshold pre-defined	Collected before oropharyngeal/nasal anterior nares	and the Xpert Xpress SARS-CoV-2 test 76 (Cepheid, Sunnyvale, CA).
		As for reference sample		
				Extraction
				Not stated
				Target
				Not stated
				Threshold
				A positive swab result was defined as SARS-CoV-2 detection in at least two NAATs. A positive diagnosis was defined as an individual being positive on any one swab.
				Threshold pre-defined
				Yes
Pere 2020	Nasal mid-turbinate	Extraction	Nasopharyngeal	RT-PCR
44 (37)	Device Manufacturer	As for reference sample	Operator	Manufacturer
	Copan Transystem, Brescia, Italy		Not stated	Allplex 2019-nCoV assay (Seegene, Seoul, Korea)
	Operator	Testing method	Collection method	Targets
	Not stated	As for reference sample	Xpert nasopharyngeal sample collection kit, Cepheid, Sunnyvale, CA, USA	Not stated
	Collection method	Target		Threshold
	Swab inserted in the nostril to the inferior concha, rotated five times, and removed.	As for reference sample		Not stated
	15 mL tube containing 3 mL of saline solution (0.9% NaCl)	Threshold	Swab inserted into the nostril at the back of the nasopharyngeal cavity, rotated five times, and removed. Xpert nasopharyngeal sample collection kit, Cepheid, Sunnyvale, CA, USA	Threshold pre-defined
		As for reference sample		Unclear
		Threshold pre-defined		
		As for reference sample	3 mL of virus transport medium	
Pham 2020	(A) Oropharyngeal	Extraction	Nasopharyngeal	RT-PCR
35 (14)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
			Not stated	

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Hologic Aptima Specimen Transport Medium (STM)	Testing method	Collection method	Hologic Panther Fusion SARS-CoV-2 RT-PCR EUA assay
	Operator	As for reference index sample	[1] BD Universal Viral	Targets
	Not stated	Target	Transport Nasopharyngeal swab and Universal Viral Transport Medium (VTM) or	Not stated
	Collection method	As for reference index sample	[2] Copan Minitip flocced swab and Viral Transport Medium	Threshold
	Sample taken after nasal swab. Posterior pharynx swabbed for 3-5 seconds and then swab placed into a specimen tube	Threshold		Not reported; highest reported Ct value was 35.3.
	Samples stored in STM, frozen and shipped for processing	As for reference index sample		Threshold predefined
	(B) Nasal mid-turbinate	Threshold predefined	Collection	Yes
	Device Manufacturer	As for reference index sample	Healthcare worker	
	Hologic Aptima Specimen Transport Medium (STM)		Swab	
	Operator		Samples stored in Viral Transport Medium, frozen and shipped	
	Not stated			
	Collection method			
	Nasal sample taken before oropharyngeal. Insert swab into nostril past inferior turbinate, approximately 3 cm, twisting the swab in mid-turbinate area for 3 to 5 seconds and place the swab into a tube of STM			
	Samples stored in STM, frozen and shipped to laboratory			
Potter 2022	Saliva spit	Extraction	Nasopharyngeal swab	RT-PCR
304 (41)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Nunc 50 mL conical (Thermo Fisher Scientific), CellPro 50mL conical (Alkali Scientific), or Corning Self-Standing 50 mL conical (Corning) tubes	Testing method	Healthcare worker	Quidel Lyra SARS-CoV-2 assay (Lyra)
	Operator	As for reference index sample	Collection method	Extraction
	Unsupervised patient	Target	Universal Transport Medium or Eswab liquid Amies transport medium	NUCLISENS-easyMAG automated extraction system
	Collection method	As for reference index sample		Target
	A small amount of saliva (approximately 1 mL) should be placed in a 50 mL conical tube, put into a plastic bag, and given to the healthcare worker collecting the nasopharyngeal swab.	Threshold	A flocced nasopharyngeal swab was collected as part of standard of care and placed into universal transport medium or ESwab	pp1ab target gene
	Patients were instructed to "spit" into a 50 mL conical tube. No specific exclusions related to food/drink consumption prior to specimen collection were provided to either cohort.	Threshold predefined		Threshold
		As for reference index sample		Not stated
				Threshold predefined
				Not stated

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Dry/direct sampling PBS was added.		liquid Amies transport medium.	
Procop 2020 224 (42)	Saliva-enhanced Device Manufacturer Not stated Operator Patient Collection method Sniff strongly to gather any nasal secretion/mucus in the oropharynx, cough to produce any phlegm, and then submit these secretions and additional saliva until the specimen reaches the premarked fill line. 3 mL requested but any volume accepted. Collected in a sterile container (urine cup) No viral transport medium used; prior to testing, viscous samples were rendered more liquid using 0.5% dithiothreitol.	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold predefined As for reference index sample	Nasopharyngeal Operator Healthcare worker Collection method Collected in a standard manner Placed in 0.9% normal saline; refrigerated at collection site and transported to laboratory in insulated coolers	MagNA Pure system (Roche Diagnostics, Indianapolis, IN); RT-PCR; CDC 2019 nCoV real-time RT-PCR diagnostic panel (4 February 2020 version) using ABI 7500 Fast Dx instruments Targets N gene (3 targets) Threshold All 3 targets required for test positive; indeterminate if < 3 targets amplified Threshold predefined Yes
Rajh 2021[A]; Rajh 2021[B]; Rajh 2021[C] Total by saliva collection method: a) Oral Rayon swab = 85 (34); b) Oral Nylon swab = 500 (147); c) Saliva drool = 190 (104)	Oral swab not otherwise specified/Rayon Device Manufacturer Not stated Operator Unsupervised patient "We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 mL and after collection, tube should be refrigerated." Collection method Rayon-tipped swab (155C, Copan Italy, Brescia, Italy) RNA stabilisation fluid Cooled on ice and frozen at -80 °C until further processing Saliva drool Device Manufacturer Microcentrifuge tubes; no other details provided	Extraction [A-C] No RNA extraction; saliva samples were heat-treated. Testing method LDT PCR using Light Cyclers 480 Real-Time PCR System (S-5/20 protocol) Target N2 and N2 genes Threshold Cq values of < 40 for N1 and N2 Threshold predefined Yes	Nasopharyngeal swab Operator Healthcare worker Collection method Viral Transport Medium No further details	RT-PCR Manufacturer LDT PCR using RGQ PCR cyclers (QIAGEN, Germantown, MD, USA) Extraction QIAcube Connect (QIAGEN, Germantown, MD, USA) and QIAamp Viral RNA Mini Kit (QIAGEN, Germantown, MD, USA) Target E and RdRP genes Threshold Samples with Cq < 38 were considered positive. Threshold predefined Yes

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Operator Unsupervised patient "We instructed the individuals that the saliva samples should be collected in the morning or at least 30 min after consumption of food or drink, the amount of saliva should be between 100 and 200 mL and after collection, tube should be refrigerated." Collection method Microcentrifuge tubes with 100 L of the RNA stabilisation buffer RNA stabilisation fluid Cooled on ice and frozen at -80 °C until further processing			
Rao 2021(a) 210 (59)	Deep throat/oropharyngeal saliva Device Manufacturer Sterile collection container; no more details provided Operator Patients self-collected; no more details provided Collection method Candidates were instructed to avoid food and water for 1 h during the collection of 2 mL of deep throat saliva Direct sampling	Extraction As for the reference standard sample Testing method As for the reference standard sample Target As for the reference standard sample Threshold As for the reference standard sample Threshold pre-defined Yes	Mixed nasopharyngeal/oropharyngeal Operator Not stated Collection method Viral Transport Medium Samples collected using sterile flocked swabs and placed in a sterile tube containing viral transport medium (VTM)	RT-PCR Manufacturer One-step RT-PCR of a DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit (Solgent Co., Ltd.) Extraction Magna Pure 96 DNA and Viral NA Small Volume extraction kit (Roche Diagnostic GmbH) Target N and ORF1a genes Threshold Samples were classified as positive for SARS-CoV-2 when either one or both gene primer-probe sets were detected at a Ct value of < 40 as per the kit's instructions. Threshold pre-defined Yes
Rao 2021 (b) 351 (5)	Deep throat/oropharyngeal saliva Device Manufacturer	Extraction As for the reference standard sample	Mixed nasopharyngeal/oropharyngeal Operator	RT-PCR Manufacturer

Table 7. Study characteristics: details of testing (index and reference samples) (a) (Continued)

	Sterile collection container; no more details provided	Testing method	Not stated	One-step RT-PCR of a DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit (Solgent Co., Ltd.)
	Operator	As for the reference standard sample	Collection method	Extraction
	Patients self-collected; no more details provided	Target	Viral Transport Medium	Magna Pure 96 DNA and Viral NA Small Volume extraction kit (Roche Diagnostic GmbH)
	Collection method	As for the reference standard sample	Samples collected using sterile flocked swabs and placed in a sterile tube containing viral transport medium (VTM)	Target
	Candidates were instructed to avoid food and water for 1 h during the collection of 2 mL of deep throat saliva	Threshold		N and ORF1a genes
	Direct sampling	As for the reference standard sample		Threshold
	As for the reference standard sample	Threshold pre-defined		Samples were classified as positive for SARS-CoV-2 when either one or both gene primer-probe sets were detected at a Ct value of < 40 as per the kit's instructions.
		Yes		Threshold pre-defined
				Yes
Sahajpal 2021	Saliva spit	Extraction	Nasopharyngeal swabs	RT-PCR
240 (68)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Sterile container (DNA/RNA Shield Saliva Sputum Collection Kit e DX, catalog number R1210-E; Zymo Research, Irvine, CA)	Testing method	Healthcare worker	TaqMan-based real time PCR assay
	Operator	As for reference index sample	Collection method	Extraction
	Patient/parent instructed but unclear if supervised	Target	3 mL of viral transport medium (Specimen Collection and Transport System BD Sterile)	Not stated
	Collection method	As for reference index sample	sterile flocked swab	Target
	Unclear (instructed but unclear if supervised)	Threshold		N and ORF1ab genes
	2 mL of viral transport medium	As for reference index sample		Threshold
		Threshold pre-defined		Both or one of the targets ≤ 42
		As for reference index sample		Threshold pre-defined
				Yes

Abbreviations

2019-nCoV: 2019-novel coronavirus

ABI: Applied Biosystems

Ag: antigen
 Ag-RDT: antigen-detection rapid diagnostic test
 BD: Becton, Dickson and Company
 BHQ-1: Black Hole Quencher®-1
 CDC: Centre for Disease Control
 CE-IVD: CE marked In Vitro Diagnostic
 CoV-2: coronavirus 2
 COVID-19: coronavirus disease 19
 Cq: quantification of cycle value
 Ct: cycle threshold
 CTAB: cetrimonium bromide
 Cy5: cyanine 5
 DHA: Defence Health Agency
 DMEM: Dulbecco's Modified Eagle Medium
 DNA: deoxyribonucleic acid
 DTT: dithiothreitol
 D+: disease-positive
 DMEM: Dulbecco's Modified Eagle Medium
 E: envelope protein
 EUA: European University Association
 FBS: foetal bovine serum
 FCS: furin cleavage sites
 FN: false negative
 FP: false positive
 GITC: guanidine thiocyanate
 h: hour
 HCW: healthcare worker
 HEPES: 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid
 iAMP: isothermal amplification
 IGI: Innovative Genomics Institute
 in: inch
 LDT: laboratory-developed test
 mM: milli mols
 min: minutes
 MEM: Minimum Essential Media
 MT: mid-turbinate
 MTM: molecular transport medium
 MWS: mouthwash saliva
 N/n: number
 N (1/2/N1): nucleocapsid gene (1/2/N1)
 NA: neuraminidase
 NAAT: Nucleic Acid Amplification Test
 NaCl: sodium chloride
 NEB: New England Biolabs
 NFS: nasopharyngeal flocced swabbing
 NP: nasopharyngeal
 OGD; Oragene Dx
 ORF1/8ab/: open reading frames 1/8ab
 OS: oral self-sampling
 PBS: phosphate buffered saline
 PCR: polymerase chain reaction
 PVA: polyvinyl acetate
 RdRp: RNA-dependent RNA polymerase
 RDT: rapid diagnostic tests
 RGQ: Rotor-Gene Q
 RLU: relative light unit
 RNA: ribonucleic acid
 RNPS: ribonucleoproteins
 RP: RNaseP (Ribonuclease P)
 RPP30: Ribonuclease P/MRP Subunit P30
 RT-/qPCR: real time-/quantitative polymerase chain reaction
 RT-PCR: reverse transcriptase polymerase chain reaction

S: spike or surface glycoprotein
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
SOC: Systems and Organisations Control
s: seconds
STM: specimen transport medium
TIB: Top International Biotech
TMA: transcription-mediated amplification
TN: true negative
TP: true positive
UTM: Universal Transport Medium
UVT: ultraviolet light transmittance
vs: versus
VTM: viral transport medium
+ve: positive
-ve: negative

Table 8. Study characteristics: details of testing (index and reference samples) (b)

Study N (n SARS-CoV-2 cases)	Index sample details	Index sample testing method	Reference sample details	REFERENCE SAMPLE TESTING METHOD
Sahni 2021 567 (114)	Nasal mid-turbinate Device Manufacturer Not stated Operator Healthcare worker (HCW) Collection method Copan-contoured nylon flocked swabs with stopper and tapered. Nasal mid-turbinate samples collected before Nasopharyngeal swab BD universal viral transport media (Becton, Dickinson and Company, Franklin Lakes, New Jersey). Specimen types were placed in 3 mL of viral transport media and placed on ice for up to 5 hours.	Extraction QIAampViral mini RNA Kit (QIAGEN Sciences, Maryland) Testing method CDC EUA of CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time reverse transcriptase polymerase chain reaction (RT-PCR) Diagnostic Panel Target N1 and N2 genes Threshold Ct value ≤ 40 Threshold predefined Yes	Nasopharyngeal Operator Healthcare worker (HCW) Collection method Several viral transport media; no more details provided Several commercial nylon and flocked swabs: Copan-contoured nylon flocked swabs (Copan Diagnostics, Murrieta, California), iClean nylon flocked swabs (Huachenyang (Shenzhen) Technology Co., Ltd, Houston, Texas), Diagnostic Hybrids flocked swabs (Diagnostic Hybrids, Quidel Corporation, San Diego, California)	RT-PCR Manufacturer RealStar® SARS-CoV-2 RT-PCR kit (Altona, Hamburg, Germany; n = 279 of 573 specimens) or Aptima® SARSCoV-2 Assay on the Hologic Panther® System (Hologic, Marlborough, Massachusetts; n = 294 of 573 specimens) Extraction MagNA Pure 96 (Roche, Indianapolis, Indiana) Target E and S genes or ORF1ab gene Threshold Ct value ≤ 45 or light reaction Threshold predefined Yes
Salvatore 2021 452 (121)	Nasal mid-turbinate swab, single nostril Device Manufacturer	Extraction	Nasopharyngeal swabs	RT-PCR Manufacturer

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

	Not stated	As for reference index sample	Operator	CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel
	Operator	Testing method	Healthcare worker	Extraction
	Unsupervised patient (instructions provided)	As for reference index sample	Collection method	The QIAgen EZ1 Advanced XL or the bio-Mérieux EMAG
	Collection method	Target	Not stated	Target
	Samples were collected from left nostril (opposite to reference sample) using BD regular flocked swabs	As for reference index sample	Nasopharyngeal specimens were collected by CDC clinicians from the patient's right nostril using BD flexible minitip flocked swabs.	N1 and N2 genes
		Threshold		Threshold
		As for reference index sample		Results were considered positive if signal was detected (cycle threshold [Ct] < 40) for RP, N1, and N2 genes
		Threshold predefined		Threshold predefined
		As for reference index sample		Specimens whose results were classified as inconclusive (either N1 or N2 was detected, but not both) were re-tested. Results were classified as invalid if RP was not detected.
Schwob 2020	Saliva swab + drool	Extraction	Nasopharyngeal swab	RT-PCR
928 (385)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated	Testing method	Healthcare worker-collected Laboratory-interpreted	In-house RT-PCR (automated molecular diagnostic platform), OR SARS-CoV-2 test of the Cobas 6800 instrument (Roche, Basel, Switzerland)
	Operator	As for reference index sample	Collection method	Extraction
	Patient/parent-collected Laboratory-interpreted	Target	Not stated	Not stated
	Collection method	As for reference index sample	Collected after saliva. No further details	Target
	Swabbing oral mucosa and finishing by drooling saliva in a tube. Collected prior to nasopharyngeal swab	Threshold		E gene Cobas 6800 NS
		As for reference index sample		Threshold
		Threshold predefined		105 copies/ml (Ct = 30)
		As for reference index sample		Threshold predefined
				Yes

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

Senok 2020	Saliva (drool)	Extraction	Nasopharyngeal	RT-PCR
401 (35)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Sterile containers	Testing method	Healthcare worker	NeoPlex COVID-19 kit (GeneMatrix, Seoul, South Korea)
	Operator	As for reference index sample	Collection method	Extraction
	Unsupervised patient	Target	Greiner Bio- One universal transport system (Greiner Bio-One, Kremsmünster, Austria)	Chemagic viral RNA extraction kit on the automated Chemagic™ 360 Nucleic Acid Extractor (PerkinElmer, Baesweiler, Germany) according to the Manufacturer's instructions
	"Healthcare personnel were trained in giving instructions to the patients for saliva collection and a unified script was used".	As for reference index sample	A COVID-19 screening protocol already in place at the facility was followed; no details provided	Target
	Collection method	Threshold		RdRp and N genes
	Patients were asked to pool saliva in their mouth for 1–2 minutes and then gently spit 2–4 mL of saliva into the provided sterile container at least one hour after the patient last consumed food, fluid, or smoked tobacco.	As for reference index sample		Threshold
	Threshold predefined			If two gene targets or only the RdRp gene target was amplified. Cycle threshold of ≤ 40 was taken as cut-off for positive result for both target genes.
	Dry/direct sampling	As for reference index sample		Threshold predefined
				Yes
Skolimowska 2020	Saliva spit	Extraction	Nasopharyngeal/oropharyngeal	RT-PCR
132 (19)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated	Testing method	Healthcare worker (trained)	One of an unspecified number of assays (from Roche, AusDiagnostics, ThermoFisher and Abbott), approved for detection of SARS-CoV-2
	Operator	As for reference index sample	Collection method	Targets
	Patient	Target	Not stated (likely Roche Cobas given collection into PCR medium)	Not stated for first tests; PCR+ samples re-run using AusDiagnostics multiplex tandem RT-PCR, targeting ORF 1ab and 8
	Collection method	As for reference index sample	Swab: both sides of the oropharynx, then nasopharynx swabbed	Threshold
	Spit into a sterile container, without preceding coughing	Threshold	4.3 mL of Roche Cobas® PCR medium	
	On receipt in the laboratory, 4.3 mL of Cobas® PCR medium was added to saliva; storage not described	As for reference index sample		
		Threshold predefined		

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

		As for reference index sample		Not stated
				Threshold pre-defined
				Yes
Smith-Jeffcoat 2021 [A&B] [A] Nasal (anterior nares) samples: 995 (78) [B] Saliva samples (not otherwise specified): 921 (73)	[A] Nasal swab (anterior nares) Device Manufacturer Not stated Operator Unsupervised patient Collection method Patients were then advised to collect anterior nasal swab (ANS) samples by inserting a mini flocked tip swab into 1 anterior naris, twirling the swab for 10 s, removing the swab and placing it directly into the other naris, and twirling again for 10 s. 3 mL universal viral transport media (Becton, Dickinson and Company) All self-collected specimens were stored at 4 °C or frozen (ANS samples only) before extraction. [B] Saliva not otherwise specified Device Manufacturer A sterile 50 mL conical centrifuge tube Operator Unsupervised patient Collection method Patients collected ≈2 mL raw saliva, after checking an infographic outlining steps for self-collection of saliva and ANS samples. Raw saliva; no more details provided All self-collected specimens were stored at 4 °C or frozen (ANS samples only) before extraction.	Extraction As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined As for reference index sample	Nasopharyngeal swab Operator Healthcare worker (HCW) Collection method 3 mL Smart Transport Medium (MedSchenker, medschenker.com) A nasopharyngeal swab (NPS) sample was collected by healthcare workers at Grady Memorial Hospital (Atlanta, Georgia, USA) using flocked foam swabs.	RT-PCR Manufacturer CDC 2019-nCoV Real-Time Reverse transcriptase PCR Diagnostic Panel Extraction Maxwell RSC Viral Total Nucleic Acid Purification Kit (Promega) Target N1 and N2 targets Threshold Cycle threshold < 40 of both N1 and N2 gene targets were considered positive Threshold pre-defined Yes
Teo 2021 (a) [A&B] 45 (29)	[A] Saliva spit Device Manufacturer Container with 2 mL of viral RNA stabilisation fluid (SAFER-Sample Stabilisation Fluid, Lucence, Singapore)	Extraction As for reference index sample Testing method	Nasopharyngeal swab Operator Healthcare worker-collect-	RT-PCR Manufacturer Laboratory-developed RT-PCR test (CDC-LDT) on an automated Cobas 6800 system

Table 8. Study characteristics: details of testing (index and reference samples) (b) *(Continued)*

	Operator	Laboratory-developed/Healthcare worker-interpreted	Extraction
	Supervised patient-collected/healthcare worker-interpreted	Laboratory-developed RT-PCR test (CDC-LDT)	Commercial kit by GeneAid Biotech Ltd
	Collection method	Fortitude 2.1 kit (MiRXES, Singapore)	Collection method
	For the collection of naso-oropharyngeal saliva samples, participants were asked to tilt their head back slightly, clear their throat and nose, and spit the saliva into the collection bottle. The steps were repeated until the required volume (2 mL) was achieved. For “naso-oropharyngeal” saliva collection, instructional videos were shown.	Target	Target
	Viral RNA stabilisation fluid	N1, N2 gene	N1, N2 gene
	Nasopharyngeal swabs and self-administered nasal swabs were collected before transfer to Lucence.	ORF1ab gene	Threshold
	[B] Single nasal anterior nares swab	Threshold	Ct < 40 for positivity
	Device Manufacturer	Ct < 38 for positivity (www.hsa.gov.sg/docs/default-source/hprg-mdb/psar-covid-19-puo-tests/mo10_mirxes-fortitude-kit-2-1.pdf)	Threshold predefined
	Not stated	Threshold predefined	Yes
	Operator	Yes	
	Supervised patient-collected/healthcare worker-interpreted	Extraction	
	Collection method	Not stated	
	Participants were instructed to insert the swab (about 1 cm) into their nostrils (one at a time), tilt their head back slightly, and rotate the swab in a circular motion for 3 times around the nasal wall. The swab was then inserted into the collection tube	Testing method	
	Viral transport medium	Fortitude 2.1 kit (MiRXES, Singapore)	
	Nasopharyngeal swabs and self-administered nasal swabs were collected before transfer to Lucence.	Target	
		ORF1ab gene	
		Threshold	
		Ct < 38 (www.hsa.gov.sg/docs/default-source/hprg-mdb/psar-covid-19-puo-tests/mo10_mirxes-fortitude-kit-2-1.pdf)	
		Threshold predefined	
		Yes	
Teo 2021 (b)	[A] Saliva spit	Extraction [A&B]	Nasopharyngeal swab
	Device Manufacturer	As for reference index sample	Manufacturer
[A&B]	Container with 2 mL of viral RNA stabilisation fluid (SAFER-Sample Stabilisation Fluid, Lucence, Singapore)	Testing method	Laboratory-developed RT-PCR test (CDC-
		Healthcare worker-collect-	

Table 8. Study characteristics: details of testing (index and reference samples) (b) *(Continued)*

	Operator	Laboratory-developed RT-PCR test (CDC-LDT)	ed/Healthcare worker-interpreted	LDT) on an automated Cobas 6800 system
	Supervised patient-collected/healthcare worker-interpreted	Fortitude 2.1 kit (MiRXES, Singapore)	Collection method	Extraction
	Collection method	Target	Viral transport medium	Commercial kit by GeneAid Biotech Ltd.
	For the collection of naso-oropharyngeal saliva samples, participants were asked to tilt their head back slightly, clear their throat and nose, and spit the saliva into the collection bottle. The steps were repeated until the required volume (2 mL) was achieved. For “naso-oropharyngeal” saliva collection, instructional videos were shown.	N1, N2 gene ORF1ab gene	Nasopharyngeal swab collection procedure was performed by a trained researcher.	Target
	Viral RNA stabilisation fluid	Threshold		Threshold
	Nasopharyngeal swabs and self-administered nasal swabs were collected before transfer to Lucence.	Ct < 38 for positivity (www.hsa.gov.sg/docs/default-source/hprg-mdb/psar-covid-19-puo-tests/mo10_mirxes-fortitude-kit-2-1.pdf)		Ct < 40 for positivity
	[B] Single nasal anterior nares swab	Threshold predefined		Threshold predefined
	Device Manufacturer	Yes		Yes
	Not stated			
	Operator			
	Supervised patient-collected/healthcare worker-interpreted			
	Collection method			
	Participants were instructed to insert the swab (about 1 cm) into their nostrils (one at a time), tilt their head back slightly, and rotate the swab in a circular motion for 3 times around the nasal wall. The swab was then inserted into the collection tube.			
	Viral transport medium			
	Nasopharyngeal swabs and self-administered nasal swabs were collected before transfer to Lucence.			
Torres 2021	Saliva spit	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
972 (104)	SDNA-1000 Saliva Collection Device (Spectrum Solutions LLC, USA)	Testing method	Healthcare worker-collected Laboratory-collected	CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel with One Step Primer Script III RT-PCR Kit (Takara Bio Inc. Japan)
	OR Sterile dry 50 mL conical vial	As for reference index sample	Collection method	
	Operator	Target	Not stated	Extraction
	Unsupervised patient-collected. Laboratory-interpreted	As for reference index sample	Self-collection of	

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

	Collection method	Threshold	nasopharyngeal swab collection	RNAAdvance Viral XP Reagent kit extraction (Beckman)
	Self-collection of saliva was performed using either the SDNA-1000 Saliva Collection Device (Spectrum Solutions LLC, USA) or a sterile dry 50 mL conical vial.	As for reference index sample		
		Threshold pre-defined		Target
		Yes		N gene (www.fda.gov/me-dia/134922/download)
				Threshold
				Ct < 40 (www.fda.gov/me-dia/134922/download)
				Threshold pre-defined
				Yes
To 2020	(A) Oral (tongue)	Extraction [A&B]	Nasopharyngeal	RT-PCR
Nasopharyngeal-tongue 501 (49)	Device Manufacturer	As for reference sample	Operator	Manufacturer
Nasopharyngeal-nasal ant 498 (50)	Copan FLOQSwab 502CS01		Healthcare worker	(Quest Diagnostics, San Juan Capistrano, CA)
Nasopharyngeal-nasal mid 504 (52)	Sample Collection	Testing method	Collection method	Targets
	Patient	As for reference sample	Polyester tipped swab on a skinny wire (Puritan 25-800-2PDBG). Pass the swab along the floor of the nose until meeting gentle resistance as the swab touches the posterior pharynx, in the nostril corresponding to the patient's dominant hand, and rotate the swab several times and withdraw.	Not stated
	Extending the tongue, and then firmly but gently brushing a nylon flocked swab along the length of the anterior 2/3 of dorsum of the tongue for 10 seconds	Targets		Threshold
		Not stated		Not stated
	As for reference sample	Threshold		Threshold pre-defined
		Not stated		Yes
	(B) Nasal mid-turbinate	Threshold pre-defined		
	Device Manufacturer	As for reference sample		
	Nylon flocked swab (MDL NasoSwab A362CS02.MDL, 56380CS01 for adults and 56780CS01 for paediatrics)			
	Sample collection			
	Patient			
	Inserting the swab in the horizontal position until gentle resistance met; leave swab in for 10-15 seconds on each side, rotating the swab; repeat in the other nostril with the same swab.			
	As for reference sample			
	(C) Nasal anterior			
	Device Manufacturer			
	Foam swab (Puritan 25-1506 1PF100)			

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

Sample collection				
Patient				
Gently insert swab in the vertical position into one nasal passage until there is gentle resistance; leave swab in place for 10-15 seconds, rotating the swab; repeat procedure on the other side with the same swab.				
As for reference sample				
Uddin 2021 596 (231)	Saliva salivate	Extraction	Nasopharyngeal swab	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Sterile container; no details provided	Testing method	Healthcare worker	iTaq universal probes one-step RT-qPCR kit
	Operator	As for reference index sample	Collection method	Extraction
	Supervised patient	Target	Viral transport medium	QIAamp viral RNA mini kit (Qiagen, Germany)
	Collection method	As for reference index sample	The nasopharyngeal swab	Target
	Healthcare workers instructed the participants to avoid taking food, drinking water, brushing teeth, washing mouth, coughing, and sniffing before saliva collection. A flocked swab was kept under the tongue for 2 to 3 min to pool the saliva in the mouth and gently spit 1 to 2 mL of saliva into a sterile container without the transport medium.	Threshold	was collected in the viral transport medium by a trained nurse according to the standard procedure described previously.	RdRp and N genes
	Dry/direct	As for reference index sample		Threshold
	Paired saliva and nasopharyngeal swab	Threshold predefined		CT values of one or both target genes were ≤ 37
	were stored in a cool box until transported to the laboratory.	As for reference index sample		Threshold predefined
				Yes
Vaz 2020 155 (73)	Saliva spit	Extraction	Nasopharyngeal/oropharyngeal	RT-PCR
	Device Manufacturer	QIAGEN QIAamp® RNA Mini Kit (diluted with PBS prior to extraction)	Operator	Manufacturer/Extraction
	Not stated	Testing method	Not stated	RT-PCR (BIOMOL OneStep/COVID-19 Kit; Paraná Molecular Biology Institute)
	Operator	RT-PCR; Charité-Berlin protocol	Collection method	Targets
	Patient	Targets	Swab	Not stated
	Collection method	E gene, RdRp	Nasopharyngeal and oropharyngeal specimens sent to a State Reference Laboratory	Threshold
	Repeatedly spit until approximately 2 mL of sample obtained, thus avoiding mucous secretions from oropharynx or lower respiratory tract (i.e. sputum). Collected in a sterile urine cup	Threshold		Not stated
	Transported to the infectious diseases research laboratory (LAPI) in a thermal box at 2 to 8 °C, and stored at -80 °C until	≤ 40 Ct; both E and RdRp targets detected		Threshold predefined
				Yes

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

	nucleic acid extraction (within 6 h of collection where possible)	Threshold pre-defined	As for reference sample	
Vermeiren 2020	Nasal mid-turbinate	Extraction	Nasopharyngeal	RT-PCR
94 (35)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	ESwab collection system; catalog no. 480C	Testing method	Not stated	BD Max System (Becton, Dickinson, USA)
	Operator	As for reference index sample	Collection method	OR Rotor-gene Q (Qiagen, Germany)
	Not stated	Target	Order not specified	Extraction
	Collection method	As for reference index sample	Nasopharyngeal sampling technique	EasyMAG (bioMérieux, France)
	'Mid-turbinate sampling' using a flocked regular nylon tip swab	Threshold	Copan Universal Transport Medium system	Targets
	liquid Amies	As for reference index sample		SARS-CoV-2 UTR'5 region OR SARS-CoV-2 UTR'5 and E gene regions
		Threshold pre-defined		Threshold
		As for reference index sample		Not stated
				Threshold pre-defined
				Yes
Villar 2020	Saliva salivate	Extraction	Nasopharyngeal	RT-PCR
13 (9)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Salivette tubes (SARSTEDT Ag & Co, Numbrecht, Germany)	Testing method	Not stated	2019-nCoV CDC EUA Kit, Integrated DNA Technologies, Coralville, USA
	Operator	As for reference index sample	Collection method	Extraction
	Patient	Target	Swab; no further details	QIAamp Viral RNA Mini Kit, QIAGEN, Germany
	Collection method	As for reference index sample		Targets
	Swab; no further details	Threshold		Not stated
		As for reference index sample		Threshold
		Threshold pre-defined		Not stated
		As for reference index sample		Threshold pre-defined
				Yes

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

Vlek 2020 107 (27)	Oropharyngeal/nasal mid-turbinate	Extraction	Nasopharyngeal	Magnapure MP24 total NA kit (Roche, Almere, the Netherlands)
	Device Manufacturer Eswab Collection system, Copan, Italy, catalog No. 490CE Operator Healthcare worker Collection method Swabs with flocked nylon fibre tip; rear wall of the oropharynx and the lower nasal cavity using the same swab 1 mL liquid Amies medium; transported to the microbiology laboratory where PCR testing was performed on the same day	As for reference index sample Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined As for reference index sample	Operator Healthcare worker Collection method Eswab Collection system, Copan, Italy, catalog No. 483C Ultra-thin applicator swab with flocked nylon fibre tip; swabbed one nostril until reaching the back of the nasopharyngeal cavity and rotated before removal 1 mL liquid Amies medium; transported to the microbiology laboratory where PCR testing was performed on the same day	RT-PCR; in-house according to Corman and colleagues (Charite-Berlin protocol) Targets Not stated Threshold < 40 Ct Threshold pre-defined Yes
Walker 2021 225 (20)	Saliva drool	Extraction	Nasopharyngeal/oropharyngeal swab	RT-PCR
	Device Manufacturer Sterile tube (SARSTEDT, USA) Operator Unsupervised patient Collection method Saliva (at least 500 µl) was collected once per week into a sterile tube (SARSTEDT, USA) by passive drool using a plastic funnel at home. Dry/direct sampling Participants were asked to store saliva samples in their home freezers (approximately -20 °C) before transportation in cooler packs (provided by the research team) to the Liverpool School of Tropical Medicine (LSTM) laboratories for processing at monthly intervals.	QIAamp Viral 143 RNA Mini Kit (Qiagen, Germany) Testing method As for reference index sample Target As for reference index sample Threshold As for reference index sample Threshold pre-defined Yes	Operator Unsupervised patient Collection method 1 mL of liquid amies (MWE, UK) Participants were asked to provide a self-collected oropharyngeal/nasal sample by swabbing the throat and then nose twice weekly when attending work.	Manufacturer Genesig® Real-150 Time Coronavirus COVID-19 PCR assay (Genesig, UK) Extraction Quick DNA/RNA™ viral 142 MagBead kit (Zymo, USA) Target Not stated Threshold Ct value < 40 Threshold pre-defined Yes
Wang 2020 353 (76)	Oropharyngeal	Extraction	Nasopharyngeal	RT-PCR
	Device Manufacturer Not stated	As for reference index sample	Operator Not reported	Manufacturer

Table 8. Study characteristics: details of testing (index and reference samples) (b) *(Continued)*

	Operator	Testing method	Collection method	(DAAN GENE; Guangzhou, China)
	Not stated	As for reference index sample	Swab collected from single nostril	Extraction
	Collection method	Target	Stored in a collection tube with 5 mL virus preservation solution	RNA was isolated with Tianlong PANA9600 automatic nucleic acid extraction system (Tianlong, Xi'an, China)
	Nasopharyngeal swab and oropharyngeal swab for each patient were taken at the same time. "A oropharyngeal swab was collected from both sides of throat according to a published video by Chinese Society of Laboratory Medicine".	As for reference index sample		RT-PCR (DAAN GENE; Guangzhou, China)
		Threshold		Targets
		As for reference index sample		N gene, ORF1ab gene
		Threshold pre-defined		Threshold
		As for reference index sample		Ct < 40 for both genes
				Threshold pre-defined
				Yes
Wehrhahn 2020 166 (13)	(A) Oropharyngeal/nasal mid-turbinate	Extraction	Nasopharyngeal/oropharyngeal	RT-PCR
	Device Manufacturer	As for reference index sample	Operator	Extraction
	Transwab® ref MW940, Medical Wire & Equipment (MWE), Wiltshire, England	Testing method	Healthcare worker	MagNA Pure 96 (Roche, Basel, Switzerland)
	Operator	As for reference index sample	Collection method	Manufacturer
	Patient	Target	Flocked nasopharyngeal swab Foam throat swab	In-house (Taqman assay)
	Collection method	As for reference index sample	Not described	Targets
	Self-collection prior to healthcare worker-collected nasopharyngeal/oropharyngeal sample. Sample kits included two swab packets each containing a single open-cell polyurethane foam swab and screw-top container with 2 mL liquid Amies medium. Oropharyngeal swabs were collected from the posterior throat and tonsil areas while nasal 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.	Threshold		E gene
	Swabs placed in separate containers with 2 mL liquid Amies medium	As for reference index sample		Threshold
	(B) Nasal mid-turbinate	Threshold pre-defined		Ct ≤ 40
	Device Manufacturer	As for reference index sample		Threshold pre-defined
	As for [A]			Yes
	Operator			

Table 8. Study characteristics: details of testing (index and reference samples) (b) (Continued)

	Patient			
	Collection method			
	As for [A]			
	(C) Oropharyngeal			
	Device Manufacturer			
	As for [A]			
	Operator			
	Patient			
	Collection method			
	As for [A]			
Williams 2020	Saliva spit	Extraction	Nasopharyngeal	RT-PCR
89 (40)	Device Manufacturer	As for reference index sample	Operator	Extraction
	Not stated		Not stated	Nucleic acid extraction on the Qiagen EZ1 platform (QIAGEN, Hilden, Germany)
	Operator	Testing method	Collection method	
	Patient	As for reference index sample	Swab	
	Collection method	Target	Median time from sample collection to addition of media was 180 minutes (range 55–537 minutes)	Manufacturer
	Pool saliva in the mouth for 1-2 minutes prior to collection, and gently spit 1-2 mL of saliva into a 25 mL collection pot	As for reference index sample		Multiplex RT-PCR test for SARS-CoV-2 and other seasonal coronaviruses (Coronavirus Typing (8-well) assay, AusDiagnostics, Mascot, Australia)
	Transported neat; approximate 1:1 ratio of liquid Amies media added	Threshold		
		As for reference index sample		
		Threshold predefined		Targets
		Yes		Not stated
				Threshold
				Not stated
				Threshold predefined
				Unclear
Zander 2021	Gargle lavage fluid	Extraction	Nasopharyngeal swab	RT-PCR
80 (26)	Device Manufacturer	As for reference index sample	Operator	Manufacturer
	Not stated		Healthcare-worker collected/laboratory staff-interpreted	Rida Gene SARS-CoV-2 assay (R-Biopharm) according to Manufacturer's instructions
	Operator	Testing method	Collection method	Extraction
	Patient-collected/laboratory staff-interpreted	As for reference index sample	Amies preservation medium (APM)	QIAcube HT, Qiagen
	Collection method	Target		

Table 8. Study characteristics: details of testing (index and reference samples) (b) *(Continued)*

Collection: performed by gargling for 30 s with 5 mL of 0.9% saline for 30 s	As for reference index sample	Collection and container: Nasopharyngeal swabs taken by professional medical staff in Copan eSwab (Copan; MAST Group) with 1 mL Amies preservation medium (APM)	Target E gene (clinical.r-bio-pharm.com/wp-content/uploads/2020/06/pg6815_rida-gene_sars-cov-2_2020-07-27_es-la_final.pdf)
Sterile saline	Threshold As for reference index sample		
	Threshold predefined Yes		Threshold The reporter emits a fluorescent signal that is detected by the optical unit of a real-time PCR. Device > 30Cq ("n= 4 positives had Cq > 30")
			Threshold predefined Yes

Abbreviations

2019-nCoV: 2019-novel coronavirus
 Ag: antigen
 ANS: anterior nasal swab
 APM: Amies preservation medium
 BD: Becton, Dickson and Company
 CDC: Centre for Disease Control
 COVID-19: coronavirus disease 19
 Cq: quantification of cycle value
 Ct: cycle threshold
 DNA: deoxyribonucleic acid
 E: envelope protein
 EUA: European University Association
 FN: false negative
 FP: false positive
 GITC: guanidine thiocyanate
 h: hour
 HCW: healthcare worker
 LDT: laboratory-developed test
 min: minutes
 N1/2: nucleocapsid gene 1/2
 N/n/No.: number
 NPS: nasopharyngeal swab
 NS: nasal sample
 ORF 1/8ab/: open reading frames 1/8ab
 PBS: Phosphate Buffered Saline
 PCR(+): polymerase chain reaction (positive)
 RdRp: RNA-dependent RNA polymerase
 RNA: ribonucleic acid
 RP: Respiratory Panel
 RT-PCR: reverse transcriptase polymerase chain reaction
 S: spike or surface glycoprotein
 s: seconds
 SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
 TMA: transcription-mediated amplification
 TN: true negative
 TP: true positive

UVT: ultraviolet light transmittance

APPENDICES

Appendix 1. Statistical method for deriving sensitivity difference

The table below shows the cross-classification of the results of the reference sample type (for example, combined NP/OP) and the alternative sample type (such as saliva, nasal swabs, etc.) for the outcome of being positive or negative for current SARS-CoV-2 infection.

		Reference sample type		
		Positive	Negative	Total
Alternative sample type	Positive	a	b	a + b
	Negative	c	d	c + d
	Total	a + c	b + d	a + b + c + d

Using the notation in the table above, the sensitivity difference (SD) was calculated as:

$$SD = (b - c) / n$$

where n is the total number who tested positive on either of the sample types.

Accounting for correlated data, the within-study variance of the sensitivity difference was calculated as follows:

$$V(SD) = \{n(b + c) - (b - c)^2\} / n^3$$

For the sensitivity analysis, in cases where variance equals to zero (due to b and c both being zero), a correction is applied where the numerator is replaced by one, making the variance the inverse of n^3 :

$$V(SD) = 1/n^3$$

Using data from the forest plot columns, the sensitivity difference can also be calculated by:

$$(positive\ on\ index\ sample - positive\ on\ reference\ sample) / total\ positive\ on\ any\ test\ (n)$$

The number of positives on the index and reference samples is equivalent to $(a + b)$ and $(a + c)$ respectively. Upon substitution of these above, we obtain

$$(a + b) - (a + c) / n\ which\ is\ equal\ to\ (b - c) / n$$

Footnotes

Abbreviations

NP/OP: nasopharyngeal or oropharyngeal; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Appendix 2. Cochrane COVID-19 register searches

Source	Strategy
CT.gov	COVID-19 ^a
WHO ICTRP	Health topic: 2019-nCov/COVID-19

(Continued)

PubMed	(("2019 nCoV"[tiab] OR 2019nCoV[tiab] OR "2019 novel coronavirus"[tiab] OR "COVID 19"[tiab] OR COVID19[tiab] OR "new coronavirus"[tiab] OR "novel coronavirus"[tiab] OR "novel corona virus"[tiab] OR "SARS CoV-2"[tiab] OR (Wuhan[tiab] AND (coronavirus[tiab] OR "corona virus"[tiab])) OR "COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) NOT (editorial[pt] OR comment[pt] OR letter[pt] OR newspaper article[pt])
Embase ^b	(coronavir* OR corona virus* OR betacoronavir* OR covid19 OR covid 19 OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR 2019nCoV OR wuhan virus*).mp. OR ((wuhan OR hubei OR huanan) AND (severe acute respiratory OR pneumonia*) AND outbreak*).mp. OR Coronavirus infection/ OR coronavirinae/ OR exp betacoronavirus/ Limits: 2020- OR (novel coronavir* OR novel corona virus* OR covid19 OR covid 19 OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR 2019nCoV OR wuhan virus*).mp. OR ((wuhan OR hubei OR huanan) AND (severe acute respiratory OR pneumonia*) AND outbreak*).mp. OR ((wuhan OR hubei OR huanan) AND (coronavir* OR betacoronavir*)).mp. Limits: 2019-

^aAutomatic term mapping links results for 2019-nCoV, 2019 novel coronavirus, SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

^bThe published Cochrane COVID-19 register currently does not display Embase records. However, Embase records obtained through Martha Knuth for the Centers for Disease Control and Prevention (CDC), Stephen B Thacker CDC Library, COVID-19 Research Articles Downloadable Database (www.cdc.gov/library/researchguides/2019novelcoronavirus/researcharticles.html) were included in the version we received from the Cochrane Central Executive Office. Embase records were deduplicated against PubMed records by Robin Featherstone from the Cochrane Central Executive Office.

Appendix 3. Living search from the University of Bern

The following information is taken from the university of Bern website (see: ispmbern.github.io/covid-19/living-review/collectingdata.html)

The register is updated daily and CSV file downloads are made available.

1 April 2020 to 17 February 2022

From 1 April 2020, we retrieved the curated BioRxiv/MedRxiv dataset (connect.medrxiv.org/relate/content/181).

26 March 2020 to 17 February 2022

MEDLINE: ("Wuhan coronavirus" [Supplementary Concept] OR "COVID-19" OR "2019 nCoV"[tiab] OR (("novel coronavirus"[tiab] OR "new coronavirus"[tiab]) AND (wuhan[tiab] OR 2019[tiab]))) OR 2019-nCoV[All Fields] OR (wuhan[tiab] AND coronavirus[tiab]))))

Embase: (nCoV or 2019-nCoV or ((new or novel or wuhan) adj3 coronavirus) or covid19 or covid-19 or SARS-CoV-2).mp.

BioRxiv/MedRxiv: nCoV or corona or wuhan or COVID or SARS-CoV-2

With the kind support of the Public Health & Primary Care Library PHC (www.unibe.ch/university/services/university_library/faculty_libraries/medicine/public_health_amp_primary_care_library_phc/index_eng.html), and following guidance of the Medical Library Association (www.mlanet.org/p/cm/ld/fid=1713).

1 January 2020 to 25 March 2020

MEDLINE: ("Wuhan coronavirus" [Supplementary Concept] OR "COVID-19" OR "2019 nCoV"[tiab] OR (("novel coronavirus"[tiab] OR "new coronavirus"[tiab]) AND (wuhan[tiab] OR 2019[tiab]))) OR 2019-nCoV[All Fields] OR (wuhan[tiab] AND coronavirus[tiab]))))

Embase: nCoV OR (wuhan AND corona) OR COVID

BioRxiv/MedRxiv: nCoV or corona or wuhan or COVID

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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Appendix 4. Search classification model

Search classification model, used from 25 May 2020

We needed a more efficient approach to keep up with the rapidly increasing volume of COVID-19 literature. A classification model for COVID-19 diagnostic studies was built with the model-building function within Eppi Reviewer, which uses the standard SGDClassifier in Scikit-learn on word trigrams. As outputs, new documents receive a percentage (from the predict_proba function), where scores close to 100 indicate a high probability of belonging to the class 'relevant document' and scores close to 0 indicate a low probability of belonging to the class 'relevant document'. We used three iterations of manual screening (title and abstract screening, followed by full-text review) to build and test classifiers. The final included studies were used as relevant documents, while the remainder of the COVID-19 studies were used as irrelevant documents. The classifier was trained on the first round of selected articles, and tested and retrained on the second round of selected articles. Testing on the second round of selected articles revealed poor positive predictive value but 100% sensitivity at a cut-off of 10. The poor positive predictive value is mainly due to the broad scope of our topic (all diagnostic studies in COVID-19), poor reporting in abstracts, and a small set of included documents. The model was retrained using the articles selected from the second and third rounds of screening, which added a considerable number of additional documents. This led to a large increase in positive predictive value, at the cost of a lower sensitivity, which led us to reduce the cut-off to 5. The largest proportion of documents had a score between 0 and 5. This set did not contain any of the relevant documents. This version of the classifier with a cut-off 5 was used in subsequent rounds and accounted for approximately 80% of the screening burden.

Appendix 5. QUADAS-2 and QUADAS-C Template

DOMAIN	SIGNALLING QUESTION	CRITERIA
PARTICIPANT SELECTION	Was a consecutive or random sample of patients enrolled?	YES: if a study explicitly stated that all participants within a certain time frame were included; that this was done consecutively; or that a random selection of participants was undertaken NO: if it was clear that a different selection procedure was employed; for example, selection based on clinician's preference, or based on institutions, or based on the result of RT-PCR UNCLEAR: if the selection procedure was not clear or not reported
	Was a case-control design avoided?	YES: if a study explicitly stated that all participants came from the same group of (suspected) patients NO: if it was clear that a different selection procedure was employed for the participants depending on their COVID-19 or SARS-CoV-2 infection status UNCLEAR: if the selection procedure was not clear or not reported
	Did the study avoid inappropriate exclusions?	YES: if samples included were likely to be representative of the spectrum of disease NO: if the study excluded patients with particular characteristics likely to affect estimates of accuracy, such as those with other diseases that might be causes of false positives UNCLEAR: if the exclusion criteria were not reported
	Did the study avoid inappropriate inclusions?	YES: if samples included were likely to be representative of the spectrum of disease NO: if the study oversampled patients with particular characteristics likely to affect estimates of accuracy, such as those with particularly low or high viral loads, or who had other diseases, such that the sample over-represented these groups UNCLEAR: if the inclusion criteria were not reported

(Continued)

	Was the intention that patients receive all tests at all time points?	YES: if authors prespecified sampling strategy, including 'stopping rules' NO: if authors described sampling as convenience or remnant samples have been used UNCLEAR: if no information provided
	Could the selection of patients have introduced bias?	HIGH: if one or more signalling questions were answered with no, as any deviation from the selection process may lead to bias LOW: if all signalling questions were answered with yes UNCLEAR: all other instances
	Is there concern that the included participants do not match the review question?	HIGH: if participants would not normally receive testing for the purposes of diagnosis LOW: for single-group studies recruiting participants with signs and symptoms of COVID-19 or asymptomatic participants with an indication for testing (e.g. contact tracing or screening) (inception cohort) UNCLEAR: if a description about the participants/setting was lacking; samples were from mixed settings; it was not clear that testing was performed for the purpose of diagnosis for all participants
INDEX TEST	If a threshold was used, was it prespecified?	YES: if the test was dichotomous by nature, or if the threshold was stated in the methods section, or if study authors stated that the threshold as recommended by the manufacturer was used NO: if a receiver operating characteristic curve was drawn or multiple thresholds reported in the results section; and the final result was based on one of these thresholds UNCLEAR: if threshold selection was not clearly reported
	Is undergoing one sample type (index test) unlikely to influence the result of the other sample type?	YES: If the order of collection of different sample types was unlikely to interfere with collection of viral material OR if the order of collection of different sample types of different sampling kits on the same sample was random NO: If sample order was not random OR if the order of collection of different sample types was likely to influence collection of viral material (for example, nasopharyngeal followed by nasal mid-turbinate in the same naris) UNCLEAR: If it was unknown whether the ordering of sample types would interfere with collection of viral material OR insufficient information was provided
	Were differences in the conduct of or interpretation of tests for each sample type (index test) unlikely to advantage one of the sample types?	YES: if PCR extraction and testing process were the same for each different sample/sample technique (e.g. nasopharyngeal and saliva samples tested with the same PCR kit) disaggregated by kit type NO: if extraction/PCR test/kit/gene target used differed for different samples UNCLEAR: if more than one PCR test/kit/gene was used but the difference in use by sample type was unclear or not reported
	If patients underwent multiple sample types (index tests), was the test result from one sample type interpreted without knowledge of	YES: if explicit mention of blinding or, from the description of study methods, interpretation of results could be assumed to have been blind NO: if blinding was not mentioned and, from the description of study methods, blinding would not be possible to achieve

(Continued)

	the test result from the other sample type?	UNCLEAR: if blinding was not mentioned and description of study methods made this difficult to judge
	Could the conduct or interpretation of the index test have introduced bias?	HIGH: if one or more signalling questions were answered with no LOW: if all signalling questions were answered with yes UNCLEAR: all other instances
	Is there concern that the index test, its conduct, or interpretation differ from the review question?	HIGH: if details of sampling procedure (order, operator, device, storage) and SARS-CoV-2 test and test kit were not provided LOW: if details of sampling procedure and test were described in full UNCLEAR: if elements of the sampling procedure and testing process were missing
FLOW AND TIMING	Was there an appropriate interval between reference and index sample types?	YES: if each sample pair was collected simultaneously or in the same clinical encounter NO: if some sample pairs were not collected within the same clinical encounter and could not be disaggregated for analysis UNCLEAR: if samples were described as paired but sample pairs could not be linked to a specific clinical encounter (e.g. data were only presented in weekly intervals)
	Did all patients receive all sample types at each time point?	YES: if data were available for all sample types for each participant NO: if data were missing for some sample types for each participant UNCLEAR: if it was not possible to link samples to participants
	Were all patients included in analysis?	YES: if all participants were included (e.g. from a STARD flow diagram) NO: if inadequate samples/indeterminate/uninterpretable results were excluded UNCLEAR: if no inadequate/indeterminate/uninterpretable results were mentioned
	Were proportions and reasons for missing data similar across sample types (index tests)?	YES: if missing data were similar across different sample types NO: if some sample types were under-represented UNCLEAR: if it was not possible to link samples to participants
	Were results presented per participant?	YES: if only one sample per participant NO: if multiple samples per participant UNCLEAR: if it was not possible to tell whether results presented were per participant or per sample
	Could the participant flow have introduced bias?	HIGH: if one or more signalling questions were answered with no LOW: if all signalling questions were answered with yes UNCLEAR: all other instances

Abbreviations

(Continued)

COVID-19: coronavirus disease 2019; PCR: polymerase chain reaction; RT-PCR: reverse transcription polymerase chain reaction; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; STARD: Standard for Reporting Diagnostic Accuracy

Appendix 6. Study characteristics summary tables

Study design and participant characteristics summary tables: [Table 5](#) and [Table 6](#).

Details of testing (index and reference samples) summary tables: [Table 7](#) and [Table 8](#).

Appendix 7. Quality assessment summaries by index sample type

[Figure 13](#): Methodological quality summary: saliva samples

Figure 13. Methodological quality summary: saliva

	Risk of Bias				Applicability Concerns		
	Patient selection	Index test: Saliva	Reference standard	Flow and timing	Patient selection	Index test: Saliva	Reference standard
AbdulRahman 2020a	?	?		?	?	+	
Aita 2020	?	?		?	?	?	
Akgun Dogan 2021	+	-		+	+	+	
Al Suwaidi 2021	?	?		?	?	+	
Altawalah 2020	?	?		-	+	+	
Babady 2021	?	?		?	?	+	
Banerjee 2021	-	-		-	+	+	
Becker 2020	?	-		-	+	+	
Bhattacharya 2021	?	?		?	+	?	
Bidkar 2022	+	-		+	+	?	
Bikos 2021	?	?		?	?	?	
Boerger 2021	?	?		?	?	?	
Borgghi 2021a	?	?		?	?	?	
Borgghi 2021c	?	?		?	?	?	
Boutros 2021(a)	+	+		+	+	+	
Boutros 2021 (b)	+	+		+	+	+	
Bruxvoort 2021	-	-		?	?	+	
Callahan 2021(e)	-	?		-	-	+	
Castelain 2021	?	?		?	?	+	
Chu 2021 (a)	?	?		?	?	?	
Chu 2021 (b)	?	?		?	?	?	
Congrave-Wilson 2021	?	+		-	?	+	
Da Costa Fernandes 2021	?	+		?	?	+	
Da Silva 2022	?	?		?	?	?	
De Oliveira 2021	?	-		-	?	?	
Desai 2021(a)[C]	?	?		-	?	?	
Desai 2021(b)	?	?		-	?	?	
Echavarria 2021	?	?		?	?	?	
Escobar 2021	?	?		?	+	+	
Faliss 2022	?	-		?	?	?	

Figure 13. (Continued)

Escobar 2021	?	?	?	+	+	
Felix 2022	?	-	?	?	?	
Fernandez-Gonzalez 2021(a)	+	?	?	+	+	
Fernandez-Gonzalez 2021(b)	+	?	?	+	+	
Fernández-Pittol 2020	?	?	?	+	+	
Fougere 2021	?	?	-	+	?	
Fronza 2021 (a)	?	+	-	?	+	
Fronza 2021 (b)	?	+	-	?	+	
Goncalves 2021	?	?	?	?	+	
Griesemer 2021 (a)	?	?	?	+	+	
Griesemer 2021 (b)	?	?	?	+	+	
Guclu 2020 (a)	-	?	?	+	+	
Guclu 2020 (b)	-	?	?	+	+	
Guzman-Ortiz 2021	-	-	-	+	+	
Hamilton 2021	?	?	?	?	?	
Herrera 2021	?	?	?	+	+	
Huber 2021 (a)	?	-	?	+	+	
Justo 2021	?	?	?	?	+	
Kannian 2021	?	?	?	?	?	
Kerneis 2021 (a)	+	?	-	+	?	
Kojima 2020	-	?	+	?	+	
Landry 2020	?	-	?	+	?	
Leung 2020	?	?	-	?	+	
Lopes 2021	?	+	?	+	+	
Mahmoud 2021	?	?	?	?	+	
Marquette 2021 (a)	+	+	+	+	+	
Marx 2021 (a)	?	?	-	?	?	
Marx 2021 (g)	?	?	-	?	?	
Matic 2021	?	-	-	?	+	
McCormick-Baw 2020	?	?	?	?	+	
McLennan 2022	?	-	-	+	+	
Melo Costa 2021 (a)	+	?	?	?	+	
Mestdagh 2021 (a)[A]	?	?	-	+	+	
Mestdagh 2021 (a)[B]	?	?	-	+	+	
Mestdagh 2021 (d)[A]	?	?	-	+	+	
Mestdagh 2021 (d)[B]	?	?	-	+	+	

Figure 13. (Continued)

Mestdagh 2021 (d)[B]	?	?		—	+	+	
Migueres 2020	?	?		?	?	?	
Migueres 2021 (a)	?	?		—	?	+	
Migueres 2021 (d)	?	?		—	?	+	
Miller 2020	—	?		?	—	+	
Moreno-Contreras 2020	?	?		?	+	?	
Nacher 2021 (a)	+	?		—	?	+	
Otto 2020	?	?		?	+	?	
Pasomsub 2020	?	+		?	+	+	
Potter 2022	?	—		—	?	?	
Procop 2020	?	?		?	+	?	
Rajh 2021[C]	?	?		?	?	+	
Rao 2021(a)	?	?		?	?	+	
Rao 2021 (b)	?	?		?	?	+	
Sahajpal 2021	?	?		—	?	+	
Schwob 2020	?	?		+	+	?	
Senok 2020	?	?		?	+	+	
Skolimowska 2020	?	?		—	+	?	
Smith-Jeffcoat 2021	+	?		?	+	+	
Teo 2021 (a)	?	?		?	+	+	
Teo 2021 (b)	?	?		?	+	+	
Torres 2021	?	?		?	+	?	
Uddin 2021	?	?		?	+	+	
Vaz 2020	?	—		?	?	?	
Villar 2020	—	?		?	?	?	
Walker 2021	—	—		—	+	+	
Williams 2020	—	?		—	+	+	

— High
? Unclear
+ Low

Figure 14: Methodological quality summary: nasal samples

Figure 14. Methodological quality summary: nasal

	Risk of Bias				Applicability Concerns		
	Patient selection	Index test: Nasal	Reference standard	Flow and timing	Patient selection	Index test: Nasal	Reference standard
Begum 2022	?	?		?	?	?	
Boerger 2021	?	?		?	?	?	
Bruxvoort 2021	—	—		?	?	+	
Callahan 2021(a)	?	?		?	?	+	
Callahan 2021(b)	—	?		—	?	+	
Callahan 2021(c)	?	?		?	?	+	
Callahan 2021(d)	?	?		?	?	+	
Chu 2021 (a)	?	?		?	?	?	
Chu 2021 (b)	?	?		?	?	?	
Cradic 2020	?	?		?	+	?	
Desai 2021(a)[A]	?	?		—	?	?	
Desai 2021(a)[B]	?	?		—	?	?	
FIND (a) 2021	+	?		?	+	?	
FIND (b) 2021	+	?		?	+	?	
FIND (c) 2021(a)	+	?		?	+	?	
FIND(c) 2021 (b)	+	?		?	+	?	
FIND(s) 2021	+	?		—	+	?	
Griesemer 2021 (a)	?	?		?	+	+	
Griesemer 2021 (b)	?	?		?	+	+	
Klein 2021	?	?		+	+	+	
Kojima 2020	—	?		+	?	+	
Labhardt 2022	+	—		—	+	+	
Lindner 2021	+	+		+	+	+	
Marx 2021 (d)	?	?		—	?	?	
Marx 2021 (m)	?	?		—	?	?	
McCulloch 2020	—	?		?	+	+	
Pere 2020	?	?		?	?	+	
Pham 2020	?	?		—	?	?	
Sahni 2021	+	?		?	+	+	
Selinger 2021	—	?		—	+	+	

Figure 14. (Continued)

Sahni 2021	+	?		?	+	+	
Salvatore 2021	-	?		-	+	+	
Smith-Jeffcoat 2021	+	-		?	+	+	
Teo 2021 (a)	?	?		?	+	+	
Teo 2021 (b)	?	?		?	+	+	
Tu 2020 [B]	?	?		-	+	?	
Tu 2020 [C]	?	?		-	+	?	
Vermeiren 2020	?	?		-	?	+	
Wehrhahn 2020	?	?		?	-	+	

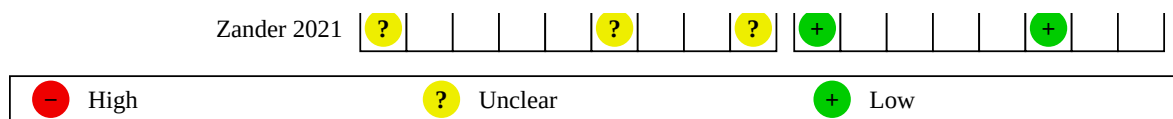
- High
? Unclear
+ Low

Figure 15: Methodological quality summary: oropharyngeal, nasal/oropharyngeal, oral rinse, operator, gargle, oral swab

Figure 15. Methodological quality summary: oropharyngeal, nasal/oropharyngeal, oral rinse, operator, gargle, oral swab

	Risk of Bias									Applicability Concerns							
	Patient selection	Index test: Oropharyngeal	Index test: Oropharyngeal/nasal	Index test: Oral rinse	Index test: Operator	Index test: Gargle	Index test: Oral swab	Reference standard	Flow and timing	Patient selection	Index test: Oropharyngeal	Index test: Oropharyngeal/nasal	Index test: Oral rinse	Index test: Operator	Index test: Gargle	Index test: Oral swab	Reference standard
Abdollahi 2020a	?				?				?	?				?			
Abdollahi 2020b	?				?				?	?				?			
Akgun Dogan 2021	+	-							+	+	+						
Amoo 2021	?				?				?	+				+			
Babady 2021	?			?					?	?			+				
Benoit 2021	?					-			-	?					+		
Cradic 2020	?	?							?	+	?						
Desmet 2020	?		?						-	+		+					
Dumaresq 2021	?					-			-	?					?		
Fernandez-Gonzalez 2021 (c)	+			?					?	+			+				
Goncalves 2021	?						?		?	?						+	
Kocagoz 2021	?					-			?	?					+		
Kojima 2020	-				-				+	?				+			
Lopes 2021	?	+							?	+	+						
Mora-Aguilera 2022 (a)	?					?			?	?					?		
Mora-Aguilera 2022 (b)	?					?			?	?					?		
Patel 2020	-	?							?	?	?						
Patriquin 2022	?		-						?	?		+					
Pham 2020	?	?							-	?	?						
Rajh 2021[A]	?						?		?	?						+	
Rajh 2021[B]	?						?		?	?						+	
Tu 2020 [A]	?						?		-	+						?	
Vlek 2020	?		?						?	+		+					
Wang 2020	?	?							?	?	+						
Wehrhahn 2020	?	?	?						?	-	+	+					
Zander 2021	?					?			?	+					+		

Figure 15. (Continued)



Appendix 8. Forest plot: investigations of heterogeneity: saliva by COVID-19 test technology; saliva by operator; nasal by time

Figure 16: Saliva samples by COVID-19 test technology

Figure 16. Forest plot: investigations of heterogeneity: saliva by COVID-19 test technology *Footnotes*

CI: confidence interval; COVID-19: coronavirus disease 19; PCR: reverse transcription polymerase chain reaction; tech: technology; TMA: transcription-mediated amplification

Study and COVID-19 test tech	Total who had both tests	Total positive on any test	Positive on saliva sample	Positive on reference sample		Sensitivity difference (95% CI)	% Weight
PCR							
AbdulRahman 2020 (a)	1009	60	47	48		-0.02 (-0.18, 0.15)	1.07
Akgun Dogan 2020	200	99	36	98		-0.63 (-0.73, -0.53)	1.24
Al Suwaidi 2021	476	80	70	74		-0.05 (-0.15, 0.05)	1.24
Altawalah 2020	889	362	305	344		-0.11 (-0.15, -0.06)	1.34
Babady 2021	87	18	17	17		0.00 (-0.15, 0.15)	1.10
Becker 2020	85	23	13	21		-0.35 (-0.61, -0.09)	0.81
Bhattacharya 2021	74	58	53	58		-0.09 (-0.16, -0.01)	1.30
Bidkar 2022	80	48	18	45		-0.56 (-0.73, -0.39)	1.05
Bikos 2021	243	70	63	65		-0.03 (-0.13, 0.07)	1.25
Boerger 2021	276	32	30	30		0.00 (-0.12, 0.12)	1.18
Borghgi 2021 (a)	192	87	60	86		-0.30 (-0.40, -0.20)	1.24
Borghgi 2021 (c)	109	27	26	21		0.19 (0.01, 0.36)	1.03
Boutros 2021 (b)	262	57	41	57		-0.28 (-0.40, -0.16)	1.20
Boutros 2021 (a)	147	59	55	58		-0.05 (-0.12, 0.02)	1.30
Bruxvoort 2021	2112	328	291	328		-0.11 (-0.15, -0.08)	1.35
Callahan 2021(e)	343	68	64	63		0.01 (-0.07, 0.10)	1.27
Castelain 2021	501	26	2	26		-0.92 (-1.03, -0.82)	1.23
Chu 2021 (a)	300	37	21	33		-0.32 (-0.54, -0.11)	0.93
Chu 2021 (b)	107	41	30	40		-0.24 (-0.39, -0.10)	1.11
Congrave-Wilson 2021	889	584	318	524		-0.35 (-0.41, -0.30)	1.33
Echavarria 2021	174	64	62	63		-0.02 (-0.07, 0.04)	1.33
Escobar 2021	127	54	51	53		-0.04 (-0.11, 0.03)	1.30
Felix 2022	50	10	8	8		0.00 (-0.39, 0.39)	0.53
Fernandes 2021	92	76	60	76		-0.21 (-0.30, -0.12)	1.26
Fernandez-Gonzalez 2021(a)	229	58	50	47		0.05 (-0.09, 0.20)	1.12
Fernandez-Gonzalez 2021(b)	208	42	28	42		-0.33 (-0.48, -0.19)	1.13
Fernández-Pittol 2020	51	38	31	37		-0.16 (-0.29, -0.02)	1.14
Fougere 2021	397	106	91	101		-0.09 (-0.18, -0.01)	1.28
Fronza 2021 (a)	193	77	65	68		-0.04 (-0.16, 0.08)	1.20
Fronza 2021 (b)	32	15	15	15		0.00 (-0.03, 0.03)	1.35
Goncalves 2021	207	85	62	78		-0.19 (-0.31, -0.07)	1.19
Griesemer 2021 (a)	236	12	6	12		-0.50 (-0.78, -0.22)	0.75
Griesemer 2021 (b)	227	93	81	91		-0.11 (-0.18, -0.03)	1.29
Guclu 2020 (a)	15	5	4	3		0.20 (-0.46, 0.86)	0.25
Guclu 2020 (b)	49	32	28	30		-0.06 (-0.21, 0.09)	1.11
Guzman-Ortiz 2021	156	23	20	17		0.13 (-0.12, 0.38)	0.83
Hamilton 2021	123	17	13	13		0.00 (-0.33, 0.33)	0.65
Herrera 2021	2107	240	172	218		-0.19 (-0.27, -0.12)	1.29
Huber 2021 (a)	1270	273	253	265		-0.04 (-0.08, -0.01)	1.35
Justo 2021	76	41	40	41		-0.02 (-0.07, 0.02)	1.34
Kannian 2021	80	57	46	55		-0.16 (-0.27, -0.04)	1.20
Kerneis 2021 (a)	1328	124	117	112		0.04 (-0.03, 0.11)	1.30
Kojima 2020	45	29	26	23		0.10 (-0.10, 0.30)	0.97
Landry 2020	124	35	30	33		-0.09 (-0.23, 0.06)	1.12
Leung 2020	95	58	51	45		0.10 (-0.05, 0.25)	1.11
Lopes 2021	1440	280	193	257		-0.23 (-0.30, -0.16)	1.30
Mahmoud 2021	595	250	216	232		-0.06 (-0.12, -0.01)	1.32
Marquette 2021 (a)	409	116	96	115		-0.16 (-0.24, -0.09)	1.30
Marx 2021 (a)	496	60	52	54		-0.03 (-0.16, 0.09)	1.18
Marx 2021 (g)	864	69	48	64		-0.23 (-0.37, -0.10)	1.15
Matic 2021	74	22	16	21		-0.23 (-0.44, -0.01)	0.92
McCormick-Baw 2020	156	50	48	49		-0.02 (-0.09, 0.05)	1.30
McLennan 2022	99	11	11	10		0.09 (-0.08, 0.26)	1.05
Melo Costa 2021 (a)	273	46	44	29		0.33 (0.17, 0.49)	1.08
Mestdagh 2021 (a)[A]	2469	118	45	105		-0.51 (-0.63, -0.38)	1.18
Mestdagh 2021 (a)[B]	2649	108	26	105		-0.73 (-0.83, -0.64)	1.25
Mestdagh 2021 (d)[A]	2491	72	40	64		-0.33 (-0.49, -0.18)	1.10
Mestdagh 2021 (d)[B]	2526	61	21	59		-0.62 (-0.76, -0.49)	1.14
Migueres 2020	123	44	37	41		-0.09 (-0.23, 0.05)	1.14
Migueres 2021 (d)	301	55	44	53		-0.16 (-0.28, -0.04)	1.19
Miller 2020	91	36	35	34		0.03 (-0.07, 0.12)	1.25
Moreno-Contreras 2020	71	34	25	28		-0.09 (-0.31, 0.13)	0.91
Nacher 2021 (a)	281	94	70	88		-0.19 (-0.30, -0.08)	1.22
Otto 2020	92	49	49	45		0.08 (0.00, 0.16)	1.29
Pasomsab 2020	200	21	18	19		-0.05 (-0.26, 0.16)	0.94
Potter 2022	304	41	29	38		-0.22 (-0.39, -0.05)	1.04
Procop 2020	223	46	46	41		0.11 (0.02, 0.20)	1.26
Rajh 2021[C]	190	104	99	104		-0.05 (-0.09, -0.01)	1.34
Rao 2021 (b)	351	5	4	4		0.00 (-0.55, 0.55)	0.33
Rao 2021 (a)	210	59	56	43		0.22 (0.09, 0.35)	1.15
Sahajpal 2021	240	68	34	61		-0.40 (-0.56, -0.24)	1.08
Schwob 2020	928	385	369	372		-0.01 (-0.04, 0.02)	1.36
Senok 2020	401	35	28	26		0.06 (-0.17, 0.28)	0.90
Skolimowska 2020	131	19	16	18		-0.11 (-0.31, 0.10)	0.96
Smith-Jeffcoat 2021	921	73	51	68		-0.23 (-0.36, -0.10)	1.17
Teo 2021 (a)	45	29	28	22		0.21 (0.03, 0.38)	1.04
Teo 2021 (b)	104	37	35	13		0.59 (0.40, 0.78)	0.99
Torres 2021	972	106	53	98		-0.42 (-0.54, -0.30)	1.19
Uddin 2021	596	231	186	229		-0.19 (-0.24, -0.13)	1.33
Vaz 2020	155	73	69	71		-0.03 (-0.09, 0.04)	1.31
Villanueva 2020	42	6	7	6		0.02 (-0.16, 0.19)	0.77

Figure 16. (Continued)

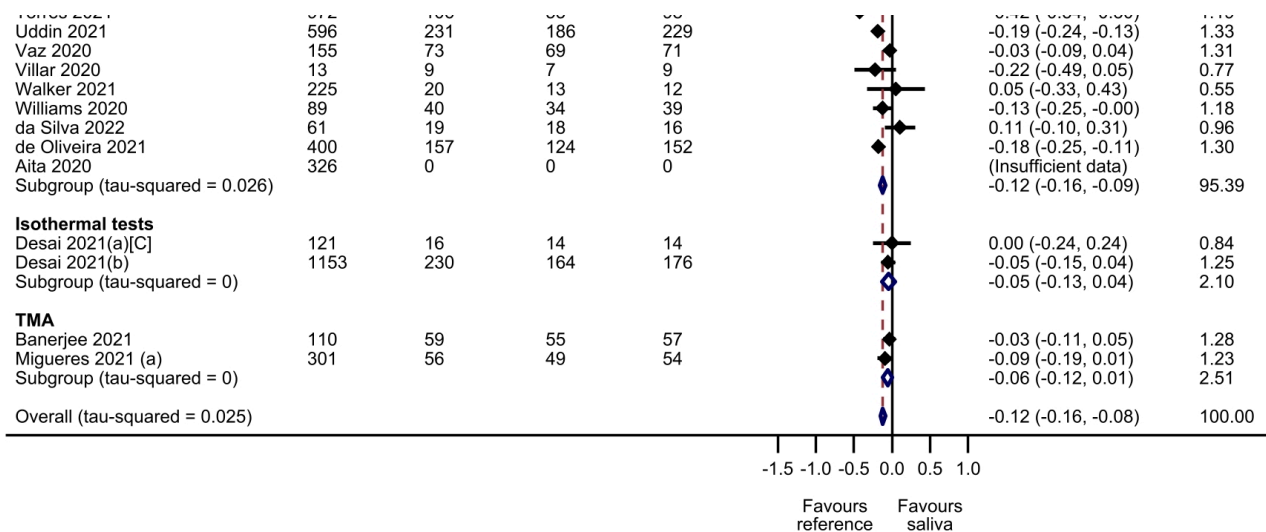


Figure 17: Saliva samples by operator

Figure 17. Forest plot: investigations of heterogeneity: saliva by operator *Footnotes*

CI: confidence interval; HCP: healthcare professional; N/A: not applicable; nos: not otherwise specified; Self: performed by patient; Self-supervised: testing supervised by a trained healthcare worker

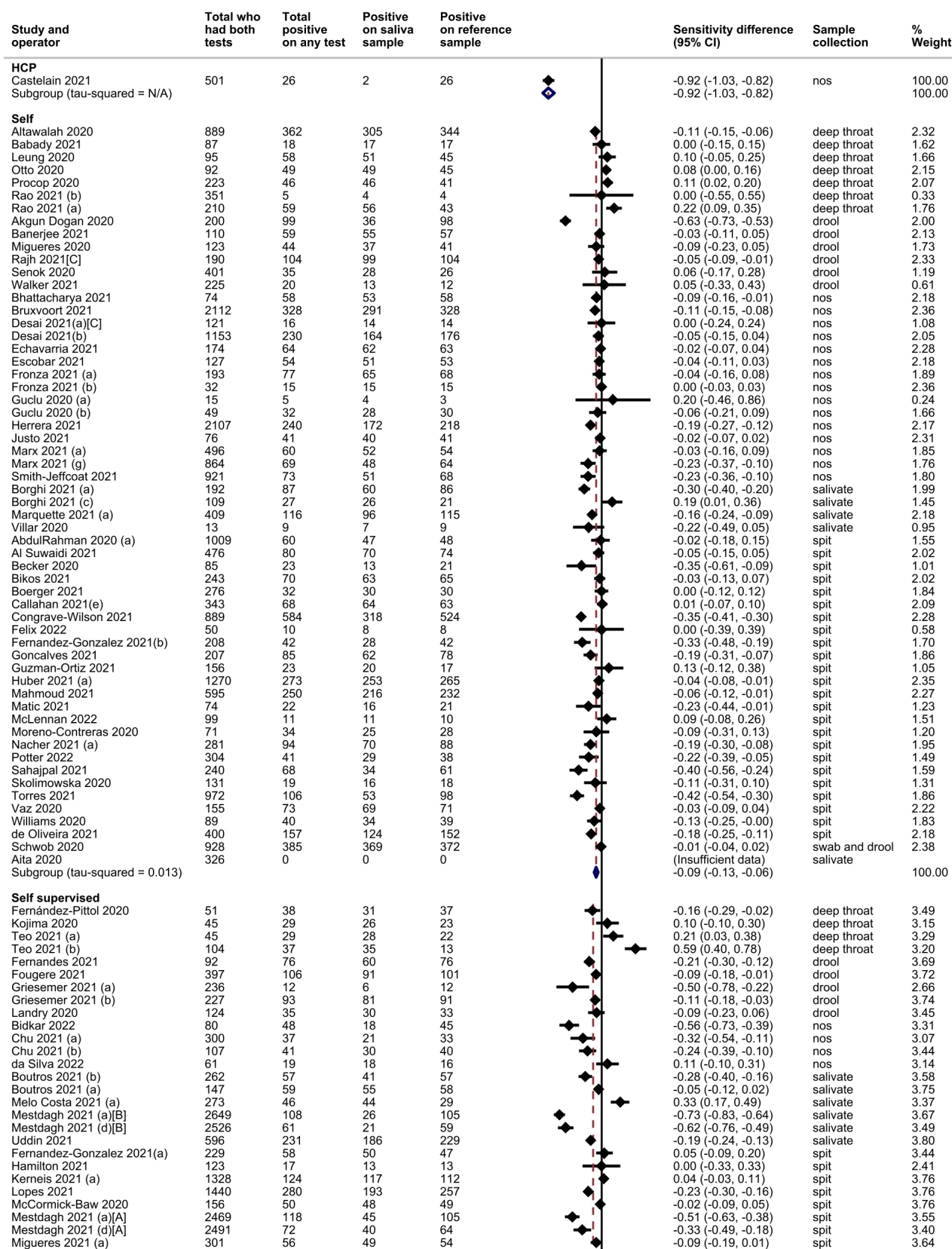


Figure 17. (Continued)

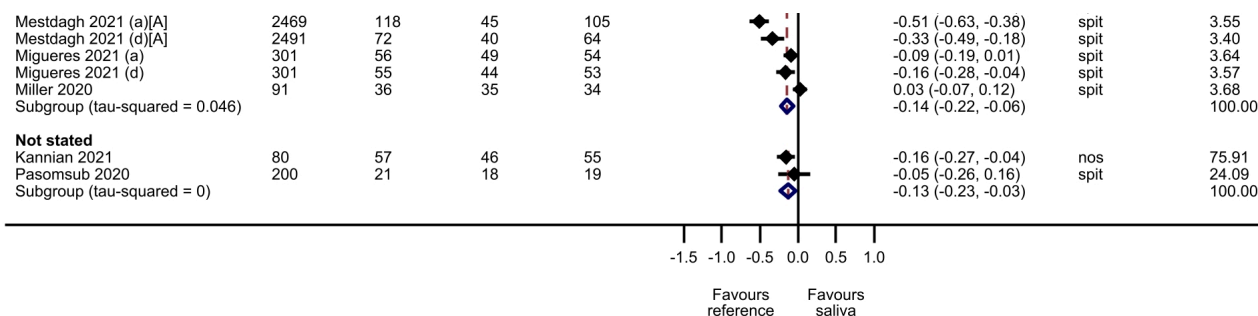
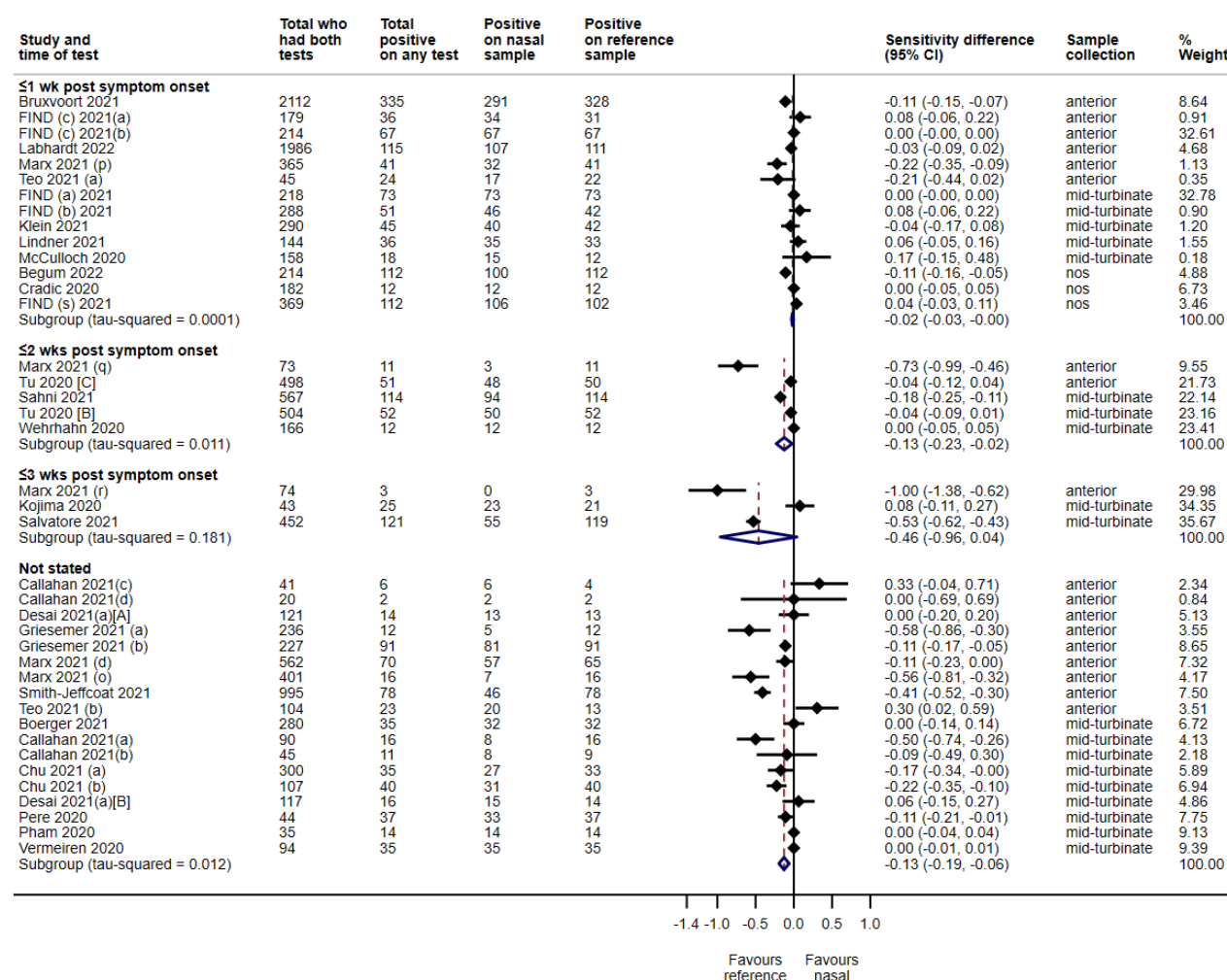


Figure 18: Nasal samples by time

Figure 18. Forest plot: investigations of heterogeneity: nasal by time *Footnotes*
CI: confidence interval; nos: not otherwise specified

Abbreviations

COVID-19: coronavirus disease 2019

Appendix 9. Summary of covariates in the nasal sample subgroup of evaluations

Group	Age				Symptom status						Time of test				Transport medium				Operator					
	Adult	Child	Mixed	Un-clear	All (age)	Symptomatic	Asymptomatic	Mixed	Un-clear	All (symptom status)	≤ 1 week PSO	≤ 2 week PSO	≤ 3 week PSO	Not stat-ified of test)	All (time-rect of test)	Direct	TM	Not stat-ed	All (transport medium)	HCW	Self-su-per-vised	Self-stat-ed	Not stat-(operator)	All
RT-PCR – overall	15	1	6	5	27	12	3	5	9	29	6	5	3	16	30	4	19	4	27	9	10	5	3	27
Ag – overall	7	0	1	0	8	4	0	4	0	8	8	0	0	0	8	1	6	1	8	2	0	1	5	8
Isothermal – overall	2	0	0	0	2	0	0	2	0	2	0	0	0	2	2	2	0	0	2	0	2	0	0	2
RT-PCR – anterior	8	0	3	0	11	5	3	3	2	13	3	2	1	8	14	2	9	0	11	4	5	2	0	11
RT-PCR – mid-turbinate	7	1	2	4	14	5	0	2	7	14	1	3	2	8	14	1	9	4	14	4	5	3	2	14
PCR – NOS	0	0	1	1	2	2	0	0	0	2	2	0	0	0	2	1	1	0	2	1	0	0	1	2
Ag – anterior	2	0	1	0	3	1	0	2	0	3	3	0	0	0	3	0	3	0	3	1	0	0	2	3
Ag – mid-turbinate	4	0	0	0	4	2	0	2	0	4	4	0	0	0	4	1	3	0	4	1	0	1	2	4
Ag – NOS	1	0	0	0	1	1	0	0	0	1	1	0	0	0	1	0	0	1	1	0	0	0	1	1
Isothermal – anterior	1	0	0	0	1	0	0	1	0	1	0	0	0	1	1	1	0	0	1	0	1	0	0	1
Isothermal – mid-turbinate	1	0	0	0	1	0	0	1	0	1	0	0	0	1	1	1	0	0	1	0	1	0	0	1
Anterior – overall	11	0	4	0	15	6	3	6	2	17	6	2	1	9	18	3	12	0	15	5	6	2	2	15
Mid-turbinate – overall	12	1	2	4	19	7	0	5	7	19	5	3	2	9	19	3	12	4	19	5	6	4	4	19
NOS – overall	1	0	1	1	3	3	0	0	0	3	3	0	0	0	3	1	1	1	3	1	0	0	2	3

Footnotes

Ag: rapid antigen test; HCP: healthcare worker; NOS: not otherwise specified; PCR: polymerase chain reaction; PSO: post-symptom onset; RT-PCR: reverse transcription polymerase chain reaction; TM: transport medium.

Appendix 10. Saliva-tabulated results: investigations of heterogeneity

Heterogeneity analysis summary tables: saliva samples by age

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2
All saliva						
Adult	50	27,987	4082	-0.12 (-0.18 to -0.07)	< 0.0001	0.035
Child	7	1468	340	0.001 (-0.07 to 0.07)	0.987	0.004
Mixed	16	6565	1837	-0.17 (-0.25 to -0.10)	< 0.0001	0.019
Unclear	18 (17)*	4322 (3996)*	1082	-0.08 (-0.13 to -0.04)	< 0.0001	0.006
<i>Difference†</i>	-				0.159	-
Deep throat						
Adult	9	1211	319	0.14 (0.01 to 0.26)	0.036	0.029
Unclear	2	981	411	-0.02 (-0.20 to 0.17)	0.869	0.017
Drool						
Adult	4	949	198	-0.17 (-0.55 to 0.22)	0.392	0.14
Child	2	507	165	-0.06 (-0.12 to -0.005)	0.034	0.0001
Mixed	3	555	181	-0.21 (-0.36 to -0.07)	0.003	0.011
Unclear	2	314	139	-0.05 (-0.09 to -0.01)	0.012	0
<i>Difference†</i>	-				0.663	-
Salivate						
Adult	7	6458	534	-0.26 (-0.48 to -0.04)	0.021	0.087
Child	1	109	27	0.19 (0.01 to 0.36)	0.042	N/A
Mixed	1	596	231	-0.19 (-0.24 to -0.13)	< 0.0001	N/A
Unclear	2 (1)	339 (13)	9	-0.22 (-0.49 to 0.05)	0.109	N/A
<i>Difference†</i>	-				0.288	-
Spit						
Adult	16	9772	1405	-0.14 (-0.21 to -0.08)	< 0.0001	0.014

(Continued)

Child	4	852	148	0.01 (-0.07 to 0.10)	0.782	0.001
Mixed	10	5207	1323	-0.13 (-0.24 to -0.02)	0.016	0.027
Unclear	6	1921	276	-0.13 (-0.26 to -0.01)	0.033	0.017
<i>Difference†</i>	-				0.079	-
Not otherwise specified						
Adult	13	8669	1241	-0.16 (-0.28 to -0.05)	0.004	0.037
Mixed	2	207	102	-0.29 (-0.81 to 0.22)	0.264	0.134
Unclear	6	767	247	-0.08 (-0.17 to 0.005)	0.063	0.008

Footnotes

*Numbers in brackets indicate those included in calculating the pooled estimates

†Comparing adult vs child estimates

Abbreviations

CI: confidence intervals; COVID-19: coronavirus disease 2019; NA: not applicable; vs: versus

Heterogeneity analysis summary tables: saliva samples by symptom status

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2
All saliva						
Symptomatic	38	13,432	2351	-0.10 (-0.15 to -0.06)	< 0.0001	0.015
Asymptomatic	18	8268	768	-0.14 (-0.33 to 0.04)	0.121	0.135
Mixed	32	12,405	3034	-0.12 (-0.19 to -0.06)	< 0.0001	0.029
Unclear	13 (12)*	3257 (2931)*	1031	-0.14 (-0.22 to -0.06)	< 0.0001	0.014
<i>Difference†</i>	-				0.705	-
Deep throat						
Symptomatic	4	411	162	0.06 (-0.06 to 0.18)	0.341	0.011
Asymptomatic	3	665	101	0.32 (0.01 to 0.64)	0.046	0.058
Mixed	2	132	47	0.04 (-0.08 to 0.16)	0.534	0
Unclear	2	984	420	-0.01 (-0.22 to 0.19)	0.890	0.019

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(Continued)

<i>Difference†</i>	-				0.133	-
Drool						
Symptomatic	3	721	240	-0.27 (-0.64 to 0.10)	0.150	0.102
Mixed	8	1604	443	-0.10 (-0.17 to -0.03)	0.004	0.005
Salivate						
Symptomatic	5	3096	228	-0.22 (-0.45 to 0.02)	0.071	0.067
Asymptomatic	6	2160	189	-0.29 (-0.59 to 0.02)	0.068	0.137
Mixed	2	705	258	-0.01 (-0.37 to 0.35)	0.954	0.064
Unclear	2 (1)*	339 (13)	9	-0.22 (-0.49 to 0.05)	0.109	N/A
<i>Difference†</i>	-				0.806	-
Spit						
Symptomatic	15	4973	633	-0.11 (-0.20 to -0.02)	0.013	0.021
Asymptomatic	5	2474	135	-0.21 (-0.79 to 0.37)	0.475	0.413
Mixed	14	7080	1868	-0.13 (-0.22 to -0.05)	0.002	0.022
Unclear	6	1447	476	-0.08 (-0.16 to 0.003)	0.060	0.008
<i>Difference†</i>	-				0.706	-
Not otherwise specified						
Symptomatic	10	3303	703	-0.06 (-0.10 to -0.02)	0.006	0.003
Asymptomatic	4	2969	343	-0.15 (-0.26 to -0.03)	0.012	0.006
Mixed	6	2884	418	-0.19 (-0.52 to 0.13)	0.236	0.156
Unclear	3	487	126	-0.38 (-0.58 to -0.18)	< 0.0001	0.023
<i>Difference†</i>	-				0.137	-

Footnotes

*Numbers in brackets indicate those included in calculating the pooled estimates

†Comparing symptomatic vs asymptomatic estimates

Abbreviations

CI: confidence intervals; COVID-19: coronavirus disease 2019; NA: not applicable; vs: versus

Heterogeneity analysis summary tables: saliva samples by time of test

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2
All saliva						
≤ 1 week post-symptom onset	21	7478	1790	-0.09 (-0.15 to -0.02)	0.006	0.015
≤ 2 weeks post-symptom onset	8	2999	622	-0.16 (-0.30 to -0.01)	0.033	0.038
≤ 3 weeks post-symptom onset	4	1473	346	-0.05 (-0.12 to 0.02)	0.172	0.002
Not stated	59 (58)*	28,232 (27,906)*	4126	-0.13 (-0.19 to -0.08)	< 0.0001	0.035
<i>Difference†</i>	-				0.574	-

Footnotes

*Numbers in brackets indicate those included in calculating the pooled estimates

†Comparison excluding 'not stated'

Abbreviations

CI: confidence intervals; COVID-19: coronavirus disease 2019

Heterogeneity analysis summary tables: saliva samples by sample collection (operator)

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2
All saliva						
Healthcare professional	1	501	26	-0.92 (-1.03 to -0.82)	< 0.0001	N/A
Self	58 (57)*	22,310 (21,984)*	5209	-0.09 (-0.13 to -0.06)	< 0.0001	0.013
Self-supervised	29	17,251	2028	-0.14 (-0.22 to -0.06)	0.001	0.046
Not stated	2	280	78	-0.13 (-0.23 to -0.03)	0.012	0
<i>Difference†</i>	-				0.0004	-
Deep throat						
Self	7	1947	597	0.06 (-0.05 to 0.17)	0.275	0.016
Self-supervised	4	245	133	0.18 (-0.14 to 0.50)	0.260	0.098

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(Continued)

Difference	-				0.392	-
Drool						
Self	6	1249	361	-0.13 (-0.34 to 0.08)	0.216	0.058
Self-supervised	5	1076	322	-0.15 (-0.23 to -0.07)	< 0.0001	0.005
Difference	-				0.729	-
Salivate						
Self	5 (4)*	1049 (723)*	239	-0.13 (-0.30 to 0.04)	0.143	0.025
Self-supervised	6	6453	562	-0.26 (-0.50 to -0.02)	0.037	0.090
Difference	-				0.552	-
Spit						
Self	24	8623	2265	-0.13 (-0.19 to -0.07)	< 0.0001	0.017
Self-supervised	10	8929	866	-0.12 (-0.23 to -0.02)	0.022	0.025
Not stated	1	200	21	-0.05 (-0.26 to 0.16)	0.653	N/A
Difference†	-				0.867	-
Not otherwise specified						
Healthcare professional	1	501	26	-0.92 (-1.03 to -0.82)	< 0.0001	N/A
Self	15	8514	1362	-0.07 (-0.11 to -0.04)	< 0.0001	0.003
Self-supervised	4	548	145	-0.26 (-0.52 to 0.002)	0.051	0.062
Not stated	1	80	57	-0.16 (-0.27 to -0.04)	0.008	N/A
Difference†	-				< 0.0001	-

Footnotes

*Numbers in brackets indicate those included in calculating the pooled estimates

†Comparison excluding 'not stated'

Abbreviations

CI: confidence intervals; COVID-19: coronavirus disease 2019; NA: not applicable

Heterogeneity analysis summary tables: saliva samples by transport medium

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2

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(Continued)

All saliva

Direct	42	16,472	3805	-0.09 (-0.13 to -0.05)	< 0.0001	0.011
TM	35 (34)*	20,162 (19,836)*	2588	-0.18 (-0.26 to -0.10)	< 0.0001	0.050
Saline	1	281	94	-0.19 (-0.30 to -0.08)	< 0.0001	N/A
Water	1	273	46	0.33 (0.17 to 0.49)	< 0.0001	N/A
Not stated	11	3154	808	-0.10 (-0.18 to -0.01)	0.024	0.014
<i>Difference†</i>	-				0.064	-

Footnotes

*Numbers in brackets indicate those included in calculating the pooled estimates

†Comparing direct vs TM estimates

Abbreviations

CI: confidence intervals; COVID-19: coronavirus disease 2019; N/A: not applicable; TM: transport medium; vs: versus

Appendix 11. Nasal-tabulated results: investigations of heterogeneity
Heterogeneity analysis summary tables: nasal samples by symptom status, time of test, transport medium and COVID-19 test technology

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2
Symptom status						
Symptomatic	16	6115	1168	-0.02 (-0.04 to -0.01)	< 0.0001	0.0002
Asymptomatic	3	837	54	-0.15 (-0.71 to 0.40)	0.583	0.214
Mixed	11	4934	604	-0.12 (-0.26 to 0.01)	0.061	0.043
Unclear	9	1093	194	-0.11 (-0.21 to -0.003)	0.045	0.015
<i>Difference†</i>	-				0.401	-
Time of test						
≤ 1 week post-symptom onset	14	6764	1077	-0.02 (-0.03 to -0.003)	0.020	0.0001
≤ 2 weeks post-symptom onset	5	1808	240	-0.13 (-0.23 to -0.02)	0.018	0.011
≤ 3 weeks post-symptom onset	3	569	149	-0.46 (-0.96 to 0.04)	0.071	0.181

(Continued)

Not stated	18	3819	551	-0.13 (-0.19 to -0.06)	< 0.0001	0.012
<i>Difference†</i>	-				0.041	-
Transport medium						
Direct	7	2741	426	-0.02 (-0.09 to 0.05)	0.610	0.004
TM	25	8730	1251	-0.04 (-0.06 to -0.03)	< 0.0001	0.0005
Not stated	5	1508	343	-0.18 (-0.42 to 0.06)	0.146	0.071
<i>Difference†</i>	-				0.400	-
COVID-19 test technology						
PCR by sample collection						
Anterior	11	5772	766	-0.16 (-0.26 to -0.06)	0.002	0.020
Mid-turbinate	14	2885	565	-0.11 (-0.18 to -0.05)	0.001	0.011
Not otherwise specified	2	396	124	-0.05 (-0.16 to 0.05)	0.329	0.005
<i>Difference†</i>	-				0.689	-
Rapid antigen test by sample collection						
Anterior	3	2379	218	-0.003 (-0.03 to 0.03)	0.831	0.0003
Mid-turbinate	4	940	205	0.00 (-0.003 to 0.003)	0.972	0
Not otherwise specified	1	369	112	0.04 (-0.03 to 0.11)	0.315	N/A
<i>Difference†</i>	-				**	-
Isothermal tests by sample collection						
Anterior	1	121	14	0.00 (-0.20 to 0.20)	1.000	N/A
Mid-turbinate	1	117	16	0.06 (-0.15 to 0.27)	0.560	N/A

Footnotes

**no P value due to model non-convergence

†excluding mixed, unclear, not stated or not otherwise specified

Abbreviations

CI: confidence intervals; COVID-19: coronavirus disease 2019; N/A: not applicable; PCR: polymerase chain reaction; TM transport medium

Heterogeneity analysis summary tables: nasal samples by sample collection (operator)

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2
All nasal						
Healthcare professional	11	3573	429	-0.09 (-0.16 to -0.01)	0.019	0.008
Self	12	6897	876	-0.14 (-0.23 to -0.04)	0.006	0.025
Self-supervised	6	889	192	-0.06 (-0.20 to 0.07)	0.336	0.018
Not stated	8	1620	523	-0.001 (-0.01 to 0.01)	0.699	0.00004
<i>Difference†</i>	-				0.787	-
Anterior						
Healthcare professional	5	2510	226	-0.11 (-0.25 to 0.04)	0.146	0.014
Self	6	5220	622	-0.19 (-0.31 to -0.06)	0.004	0.021
Self-supervised	2	149	47	0.04 (-0.46 to 0.54)	0.872	0.114
Not stated	2	393	103	0.01 (-0.04 to 0.06)	0.705	0.001
<i>Difference†</i>	-				0.591	-
Mid-turbinate						
Healthcare professional	5	881	191	-0.11 (-0.25 to 0.02)	0.101	0.017
Self	6	1677	254	-0.08 (-0.25 to 0.10)	0.387	0.039
Self-supervised	4	740	145	-0.10 (-0.22, 0.03)	0.126	0.010
Not stated	4	644	196	-0.001 (-0.01 to 0.01)	0.902	0.00003
<i>Difference†</i>	-				0.925	-
Not otherwise specified						
Healthcare professional	1	182	12	0.00 (-0.05 to 0.05)	1.000	N/A
Not stated	2	583	224	-0.04 (-0.18 to 0.10)	0.603	0.009
<i>Footnotes</i>						
†comparisons excluding 'not stated'						
<i>Abbreviations</i>						
CI: confidence intervals; COVID-19: coronavirus disease 2019; NA: not applicable						

Appendix 12. Sensitivity analysis

SAME COVID-19 TEST KIT: ALL SAMPLE TYPES

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ^2
Saliva	80 (79)*	36,599 (36,273)*	6601	-0.12 (-0.16 to -0.08)	< 0.0001	0.027
<i>By COVID-19 test tech</i>						
PCR	76 (75)*	34,914 (34,588)*	6240	-0.12 (-0.16 to -0.08)	< 0.0001	0.028
Isothermal	2	1274	246	-0.05 (-0.13 to 0.04)	0.305	0
TMA	2	411	115	-0.06 (-0.12 to 0.01)	0.088	0
<i>Difference</i>	-				<i>0.822</i>	-
<i>By sample collection</i>						
Deep throat	11	2192	730	0.10 (-0.01 to 0.21)	0.068	0.027
Drool	10	2135	579	-0.17 (-0.30 to -0.04)	0.011	0.038
Salivate	11 (10)*	7502 (7176)*	801	-0.21 (-0.37 to -0.05)	0.011	0.062
Spit	29	16,713	2834	-0.14 (-0.19 to -0.08)	< 0.0001	0.020
Swab and drool	1	928	385	-0.01 (-0.04 to 0.02)	0.577	N/A
Not otherwise specified	18	7129	1272	-0.14 (-0.22 to -0.06)	0.001	0.028
<i>Difference†</i>	-				<i>0.0106</i>	-
Nasal	32	11,795	1782	-0.05 (-0.07, -0.04)	< 0.0001	0.001
<i>By COVID-19 test tech</i>						
PCR + isothermal	24	8107	1247	-0.11 (-0.17 to -0.06)	< 0.0001	0.013
Rapid antigen test (Ag)	8	3688	535	0.00 (-0.002 to 0.002)	0.974	0
<i>Difference</i>	-				<i>0.094</i>	-
<i>By sample collection</i>						
Anterior	15	8272	998	-0.11 (-0.18 to -0.04)	0.002	0.013

(Continued)

Mid-turbinate	14	2758	548	-0.04 (-0.08 to -0.01)	0.010	0.001
Not otherwise specified	3	765	236	-0.02 (-0.11 to 0.06)	0.547	0.004
<i>Difference†</i>	-				0.543	-
Oropharyngeal (OP)	6	2356	499	-0.18 (-0.32 to -0.05)	0.007	0.024
Gargle	4	2093	376	-0.02 (-0.06 to 0.02)	0.365	0.001
Oral swab	2	658	78	-0.42 (-1.12 to 0.29)	0.248	0.254

*numbers in brackets indicate those included in calculating the pooled estimates

†excluding mixed, unclear, not stated or not otherwise specified

Abbreviations

CI: confidence intervals; COVID-19: coronavirus disease 2019; N/A: not applicable; PCR: polymerase chain reaction; TMA: transcription-mediated amplification

WITHOUT CORRECTION TO WITHIN-STUDY VARIANCE: ALL SAMPLE TYPES

Group	Number of evaluations	Number of sample pairs (participants)	Number of COVID-19 cases	Difference in sensitivity (95% CI)	P value	τ ²
Saliva	90 (88)*	40,342 (39,984)*	7341 (7326)*	-0.12 (-0.16 to -0.08)	< 0.0001	0.026
<i>By COVID-19 test tech</i>						
PCR	86 (84)*	38,657 (38,299)*	6980 (6965)	-0.13 (-0.16 to -0.09)	< 0.0001	0.027
Isothermal	2	1274	246	-0.05 (-0.13 to 0.04)	0.305	0
TMA	2	411	115	-0.06 (-0.12 to 0.01)	0.088	0
<i>Difference</i>	-				0.791	-
<i>By sample collection</i>						
Deep throat	11	2192	730	0.10 (-0.01 to 0.21)	0.068	0.027
Drool	11	2325	683	-0.16 (-0.27 to -0.05)	0.005	0.028
Salivate	11 (10)*	7502 (7176)*	801	-0.21 (-0.37 to -0.05)	0.011	0.062
Spit	35	17,752	3152	-0.13 (-0.18 to -0.08)	< 0.0001	0.018
Swab and drool	1	928	385	-0.01 (-0.04 to 0.02)	0.577	N/A

The effect of sample site and collection procedure on identification of SARS-CoV-2 infection (Review)

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(Continued)

Not otherwise specified	21 (20)*	9643 (9611)*	1590 (1575)*	-0.16 (-0.25 to -0.08)	< 0.0001	0.031
<i>Difference†</i>	-				0.008	-
Nasal	37 (30)*	12,979 (12,050)*	2020 (1805)*	-0.11 (-0.16 to -0.05)	< 0.0001	0.018
<i>By COVID-19 test tech</i>						
PCR + isothermal	29 (24)*	9291 (8794)*	1485 (1410)*	-0.14 (-0.21 to -0.08)	< 0.0001	0.019
Rapid antigen test (Ag)	8 (6)*	3688 (3256)*	535 (395)*	0.01 (-0.03 to 0.06)	0.524	0.0005
<i>Difference</i>	-				0.061	-
<i>By sample collection</i>						
Anterior	15 (13)*	8272 (8038)*	998 (929)*	-0.12 (-0.20 to -0.04)	0.005	0.017
Mid-turbinate	19 (15)*	3942 (3429)*	786 (652)*	-0.10 (-0.20 to -0.01)	0.038	0.029
Not otherwise specified	3 (2)*	765 (583)*	236 (224)*	-0.04 (-0.18 to 0.10)	0.603	0.009
<i>Difference†</i>	-				0.863	-
Oropharyngeal (OP)	7 (6)*	2522 (2340)*	511 (499)*	-0.20 (-0.33 to -0.08)	0.002	0.021
Gargle	6 (5)*	2138 (2058)*	389 (363)*	-0.03 (-0.09 to 0.03)	0.345	0.002

*numbers in brackets indicate those included in calculating the pooled estimates

†Excluding mixed, unclear, not stated or not otherwise specified

Abbreviations:

CI: confidence interval; COVID-19: coronavirus disease 2019; N/A: not applicable; PCR: polymerase chain reaction; TMA: transcription-mediated amplification

CONTRIBUTIONS OF AUTHORS

CD was the contact person with the editorial base.

CD co-ordinated contributions from the co-authors and wrote the final draft of the review.

RS conducted the literature searches.

CD, JDi, YT, IA-R, AC, DB-G, MM-H screened papers against eligibility criteria.

CD, JDi, IA-R, AC, DB-G, MM-H extracted data for the review.

CD, JDi, IA-R, AC, DB-G, MM-H appraised the quality of papers.

CD, IA-R, MM-H entered data into Review Manager 2020.

CD, SB, YT and JDi analysed and interpreted data.

CD, JJD, JDi, YT, IA-R, AC, DB-G, MM-H, DE, A VdB, MML worked on the methods sections and commented on the draft review.

CD, SB and MM-H responded to the comments of the referees.

Cochrane COVID-19 Diagnostic Test Accuracy Group contributed methodological advice as part of the planning and execution of the review and commented on the final review draft.

DECLARATIONS OF INTEREST

Jonathan J Deeks*: none known.

Jacqueline Dinnes (JD)* is a Cochrane DTA Editor. She was not involved in the editorial process for this review. JD declares a grant from Evidence Synthesis Ireland, National University of Ireland, Galway, to supervise three fellows contributing to a Cochrane review of rapid antigen tests for Covid-19; paid to the institution. JD declares publishing opinions on the topic: (1) Dinnes J, Davenport C. COVID-19 rapid antigen testing strategies must be evaluated in intended use settings. *Lancet. Regional Health, Western Pacific* 2022;25:100542. DOI: 10.1016/j.lanwpc.2022.100542; (2) Deeks JJ, Dinnes J, Davenport C, Takwoingi Y, Mclnnes M, Leeflang MM, Cunningham J. Letter to the Editor regarding Peto T; UK COVID-19 Lateral Flow Oversight Team: COVID-19: Rapid antigen detection for SARS-CoV-2 by lateral flow assay. *EClinicalMedicine* 2021;38; (3) Dinnes J. COVID-19 rapid antigen testing strategies require careful evaluation. *EBioMedicine* 2021;70:103491; and (4) Dinnes J, Davenport C. Do we have informed consent for asymptomatic COVID-19 testing in schools? *BMJ Opinion*. Available at <https://blogs.bmj.com/bmj/2021/03/16/do-we-have-informed-consent-for-asymptomatic-testing-in-schools/>, 2021 [<https://blogs.bmj.com/bmj/2021/03/16/do-we-have-informed-consent-for-asymptomatic-testing-in-schools/>, 2021].

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Sarah Berhane* is employed as a medical statistician via grant funding from NIHR Birmingham Biomedical Research Centre to the University of Birmingham.

Ann Van den Bruel: none known.

Devy Emperador: is employed by FIND, with funding from FCDO and CAN. FIND is a global non-for-profit product development partnership and WHO Diagnostic Collaboration Centre. It is FIND's role to accelerate access to high-quality diagnostic tools for low-resource settings and this is achieved by supporting both research and development and access activities for a wide range of diseases, including COVID-19. FIND has several clinical research projects to evaluate multiple new diagnostic tests against published Target Product Profiles that have been defined through consensus processes. These studies are for diagnostic products developed by private sector companies who provide access to know-how, equipment/reagents, and contribute through unrestricted donations as per FIND policy and external SAC review (i.e. these companies donate these tests to FIND for free for Find-sponsored research studies).

Ingrid Arevalo-Rodriguez: none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None

INDEX TERMS

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*COVID-19 [diagnosis]; COVID-19 Nucleic Acid Testing [methods]; COVID-19 Testing [methods]; Nasal Cavity [virology]; *Nasopharynx [virology]; Nose [virology]; Oropharynx [virology]; Pharynx [virology]; *SARS-CoV-2 [isolation & purification]; *Sensitivity and Specificity; *Specimen Handling [methods]; Viral Load

MeSH check words

Humans