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[Diagnostic Test Accuracy Review]

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection

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ABSTRACT

Background

Accurate rapid diagnostic tests for SARS-CoV-2 infection would be a useful tool to help manage the COVID-19 pandemic. Testing strategies that use rapid antigen tests to detect current infection have the potential to increase access to testing, speed detection of infection, and inform clinical and public health management decisions to reduce transmission. This is the second update of this review, which was first published in 2020.

Objectives

To assess the diagnostic accuracy of rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection. We consider accuracy separately in symptomatic and asymptomatic population groups. Sources of heterogeneity investigated included setting and indication for testing, assay format, sample site, viral load, age, timing of test, and study design.

Search methods

We searched the COVID-19 Open Access Project living evidence database from the University of Bern (which includes daily updates from PubMed and Embase and preprints from medRxiv and bioRxiv) on 08 March 2021. We included independent evaluations from national reference laboratories, FIND and the Diagnostics Global Health website. We did not apply language restrictions.

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Selection criteria

We included studies of people with either suspected SARS-CoV-2 infection, known SARS-CoV-2 infection or known absence of infection, or those who were being screened for infection. We included test accuracy studies of any design that evaluated commercially produced, rapid antigen tests. We included evaluations of single applications of a test (one test result reported per person) and evaluations of serial testing (repeated antigen testing over time). Reference standards for presence or absence of infection were any laboratory-based molecular test (primarily reverse transcription polymerase chain reaction (RT-PCR)) or pre-pandemic respiratory sample.

Data collection and analysis

We used standard screening procedures with three people. Two people independently carried out quality assessment (using the QUADAS-2 tool) and extracted study results. Other study characteristics were extracted by one review author and checked by a second. We present sensitivity and specificity with 95% confidence intervals (CIs) for each test, and pooled data using the bivariate model. We investigated heterogeneity by including indicator variables in the random-effects logistic regression models. We tabulated results by test manufacturer and compliance with manufacturer instructions for use and according to symptom status.

Main results

We included 155 study cohorts (described in 166 study reports, with 24 as preprints). The main results relate to 152 evaluations of single test applications including 100,462 unique samples (16,822 with confirmed SARS-CoV-2). Studies were mainly conducted in Europe (101/152, 66%), and evaluated 49 different commercial antigen assays. Only 23 studies compared two or more brands of test.

Risk of bias was high because of participant selection (40, 26%); interpretation of the index test (6, 4%); weaknesses in the reference standard for absence of infection (119, 78%); and participant flow and timing 41 (27%). Characteristics of participants (45, 30%) and index test delivery (47, 31%) differed from the way in which and in whom the test was intended to be used. Nearly all studies (91%) used a single RT-PCR result to define presence or absence of infection.

The 152 studies of single test applications reported 228 evaluations of antigen tests. Estimates of sensitivity varied considerably between studies, with consistently high specificities. Average sensitivity was higher in symptomatic (73.0%, 95% CI 69.3% to 76.4%; 109 evaluations; 50,574 samples, 11,662 cases) compared to asymptomatic participants (54.7%, 95% CI 47.7% to 61.6%; 50 evaluations; 40,956 samples, 2641 cases). Average sensitivity was higher in the first week after symptom onset (80.9%, 95% CI 76.9% to 84.4%; 30 evaluations, 2408 cases) than in the second week of symptoms (53.8%, 95% CI 48.0% to 59.6%; 40 evaluations, 1119 cases). For those who were asymptomatic at the time of testing, sensitivity was higher when an epidemiological exposure to SARS-CoV-2 was suspected (64.3%, 95% CI 54.6% to 73.0%; 16 evaluations; 7677 samples, 703 cases) compared to where COVID-19 testing was reported to be widely available to anyone on presentation for testing (49.6%, 95% CI 42.1% to 57.1%; 26 evaluations; 31,904 samples, 1758 cases). Average specificity was similarly high for symptomatic (99.1%) or asymptomatic (99.7%) participants.

We observed a steady decline in summary sensitivities as measures of sample viral load decreased.

Sensitivity varied between brands. When tests were used according to manufacturer instructions, average sensitivities by brand ranged from 34.3% to 91.3% in symptomatic participants (20 assays with eligible data) and from 28.6% to 77.8% for asymptomatic participants (12 assays). For symptomatic participants, summary sensitivities for seven assays were 80% or more (meeting acceptable criteria set by the World Health Organization (WHO)). The WHO acceptable performance criterion of 97% specificity was met by 17 of 20 assays when tests were used according to manufacturer instructions, 12 of which demonstrated specificities above 99%. For asymptomatic participants the sensitivities of only two assays approached but did not meet WHO acceptable performance standards in one study each; specificities for asymptomatic participants were in a similar range to those observed for symptomatic people.

At 5% prevalence using summary data in symptomatic people during the first week after symptom onset, the positive predictive value (PPV) of 89% means that 1 in 10 positive results will be a false positive, and around 1 in 5 cases will be missed. At 0.5% prevalence using summary data for asymptomatic people, where testing was widely available and where epidemiological exposure to COVID-19 was suspected, resulting PPVs would be 38% to 52%, meaning that between 2 in 5 and 1 in 2 positive results will be false positives, and between 1 in 2 and 1 in 3 cases will be missed.

Authors' conclusions

Antigen tests vary in sensitivity. In people with signs and symptoms of COVID-19, sensitivities are highest in the first week of illness when viral loads are higher. Assays that meet appropriate performance standards, such as those set by WHO, could replace laboratory-based RT-PCR when immediate decisions about patient care must be made, or where RT-PCR cannot be delivered in a timely manner. However, they are more suitable for use as triage to RT-PCR testing. The variable sensitivity of antigen tests means that people who test negative may still be infected. Many commercially available rapid antigen tests have not been evaluated in independent validation studies.

Evidence for testing in asymptomatic cohorts has increased, however sensitivity is lower and there is a paucity of evidence for testing in different settings. Questions remain about the use of antigen test-based repeat testing strategies. Further research is needed to evaluate the effectiveness of screening programmes at reducing transmission of infection, whether mass screening or targeted approaches including schools, healthcare setting and traveller screening.

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

PLAIN LANGUAGE SUMMARY

How accurate are rapid antigen tests for diagnosing COVID-19?

Key messages

- Rapid antigen tests are most accurate when they are used in people who have signs or symptoms of COVID-19, especially during the first week of illness. People who test negative may still be infected.
- Rapid antigen tests are considerably less accurate when they are used in people with no signs or symptoms of infection, but do perform better in people who have been in contact with someone who has confirmed COVID-19.
- The accuracy of rapid antigen tests varies between tests that are produced by different manufacturers and there is a lack of evidence for many commercially available tests.

What are rapid point-of-care antigen tests for COVID-19?

Rapid point-of-care tests aim to confirm or rule out COVID-19 infection in people with or without COVID-19 symptoms. They:

- are portable, so they can be used wherever the patient is (at the point-of-care) or in non-healthcare settings such as in the home;
- are easy to perform, with a minimum amount of extra equipment or complicated preparation steps;
- are less expensive than standard laboratory tests;
- do not require a specialist operator or setting; and
- provide results ‘while you wait’.

For this review we were interested in rapid antigen tests, sometimes referred to as ‘lateral flow tests’. These tests identify proteins on the virus in samples taken from the nose or throat. They come in disposable plastic cassettes, similar to over-the-counter pregnancy tests.

Why is this question important?

People with suspected COVID-19 need to know quickly whether they are infected, so that they can self-isolate, receive treatment, and inform close contacts. Currently, COVID-19 infection is confirmed by a laboratory test called RT-PCR, which uses specialist equipment and often takes at least 24 hours to produce a result.

In many places, rapid antigen tests have opened access to testing for many more people, with and without symptoms, and in locations other than healthcare settings. Faster diagnosis of COVID-19 infection could allow people to take appropriate action more quickly, with the potential to reduce the spread of COVID-19, but it is important to understand how accurate they are and the best way to use them.

What did we want to find out?

We wanted to know whether commercially available, rapid point-of-care antigen tests are accurate enough to diagnose COVID-19 infection reliably, and to find out if accuracy differs in people with and without symptoms.

What did we do?

We looked for studies that measured the accuracy of any commercially produced rapid antigen test in people who were also tested for COVID-19 using RT-PCR. People could be tested in hospital, in the community or in their own homes. Studies could test people with or without symptoms.

What did we find?

We included 155 studies in the review. The main results are based on 152 studies investigating a total of 100,462 nose or throat samples; COVID-19 was confirmed in 16,822 of these samples. Studies investigated 49 different antigen tests. Around 60% of studies took place in Europe.

Main results

In people with confirmed COVID-19, antigen tests correctly identified COVID-19 infection in an average of 73% of people with symptoms, compared to 55% of people without symptoms. Tests were most accurate when used in the first week after symptoms began (an average of 82% of confirmed cases had positive antigen tests). This is likely to be because people have the most virus in their system in the first days after they are infected. For people with no symptoms, tests were most accurate in people likely to have been in contact with a case of COVID-19 infection (an average of 64% of confirmed cases had positive antigen tests).

In people who did not have COVID-19, antigen tests correctly ruled out infection in 99.6% of people with symptoms and 99.7% of people without symptoms.

Different brands of tests varied in accuracy. Summary results (combined from more than one study per test brand) for seven tests met World Health Organization (WHO) standards as 'acceptable' for confirming and ruling out COVID-19 in people with signs and symptoms of COVID-19. Two more tests met the WHO acceptable standard in one study each. No test met this standard when evaluated in people without symptoms.

Using summary results for symptomatic people tested during the first week after symptoms began, if 1000 people with symptoms had the antigen test, and 50 (5%) of them really had COVID-19:

- 45 people would test positive for COVID-19. Of these, 5 people (11%) would not have COVID-19 (false positive result).
- 955 people would test negative for COVID-19. Of these, 10 people (1.0%) would actually have COVID-19 (false negative result).

In people with no symptoms of COVID-19 the number of confirmed cases is expected to be much lower than in people with symptoms. Using summary results for people with no known exposure to COVID-19 in a bigger population of 10,000 people with no symptoms, where 50 (0.5%) of them really had COVID-19:

- 62 people would test positive for COVID-19. Of these, 30 people (48%) would not have COVID-19 (false positive result).
- 9938 people would test negative for COVID-19. Of these, 18 people (0.2%) would actually have COVID-19 (false negative result).

What are the limitations of the evidence?

In general, studies used relatively rigorous methods, particularly for selecting participants and performing the tests. Sometimes studies did not perform the test on the people for whom it was intended and did not follow the manufacturers' instructions for using the test. Sometimes the tests were not carried out at the point of care. Studies used less rigorous methods for confirming the presence or absence of COVID-19 infection; 91% of studies relied on a single negative RT-PCR result as evidence of no COVID-19 infection. Results from different test brands varied, and relatively few studies directly compared one test brand with another. Finally, not all studies gave enough information about their participants for us to judge how long they had had symptoms, or even whether or not they had symptoms.

What does this mean?

In people with symptoms, some rapid antigen tests are accurate enough to replace RT-PCR, especially for ruling in the presence of infection. Alternatively, where RT-PCR is available, rapid antigen tests could be used to select which people with symptoms require further testing with RT-PCR, thereby reducing the burden on laboratory services. This would be most useful when quick decisions are needed about patient care, to identify outbreaks, to allow people to self-isolate more quickly, or to initiate contact tracing. Rapid antigen tests are less good at ruling out infection in symptomatic people - individuals who receive a negative rapid antigen test result may still be infected.

Rapid antigen tests are less accurate when used in people with no symptoms of COVID-19. More evidence is needed to understand the accuracy of rapid testing in people without symptoms and the extent to which repeated testing strategies can lead to reduced transmission, either for tests carried out at home or in non-healthcare settings such as schools. There is no independent evidence to support the use of many test brands. More direct comparisons of test brands are needed, with testers following manufacturers' instructions.

How up-to-date is this review?

This review updates our previous review and includes evidence published up to 8 March 2021.

SUMMARY OF FINDINGS

Summary of findings 1. Diagnostic accuracy of point-of-care antigen tests for the diagnosis of SARS-CoV-2 infection

Question	What is the diagnostic accuracy of rapid point-of-care antigen tests for the diagnosis of SARS-CoV-2 infection?			
Population	Adults or children with suspected: <ul style="list-style-type: none"> current SARS-CoV-2 infection or populations undergoing screening for SARS-CoV-2 infection, including <ul style="list-style-type: none"> asymptomatic contacts of confirmed COVID-19 cases community screening 			
Index test	Any commercially produced rapid antigen test for diagnosis of SARS-CoV-2 meeting the following criteria: <ul style="list-style-type: none"> portable or mains-powered device minimal sample preparation requirements minimal biosafety requirements no requirement for a temperature-controlled environment test results available within 2 hours of sample collection 			
Target condition	Detection of current SARS-CoV-2 infection			
Reference standard	For COVID-19 cases: positive molecular-based test result (PCR or TMA) For non-COVID-19 cases: negative molecular test result or pre-pandemic sources of samples			
Action	<p>False negative results mean missed cases of COVID-19 infection, with either delayed or no confirmed diagnosis and increased risk of community transmission due to false sense of security</p> <p>False positive results lead to unnecessary self-isolation or quarantine, and may increase the potential for an infection to be acquired if individuals erroneously believe themselves to be immune</p>			
Quantity of evidence (based on 152 studies);	Population	Number of studies	Total samples	Samples from confirmed SARS-CoV-2 cases
<ul style="list-style-type: none"> 135 reporting sensitivity and specificity 16 reporting sensitivity only 1 reporting specificity only 	Any symptom status	152	100,462	16,822
	Population	Number of test evaluations (≥ 1 per study)	Total samples	Samples from confirmed SARS-CoV-2 cases

	Any symptom status	210	120,381	23,488
	Symptomatic	133	53,589	14,027
	Asymptomatic	56	41,129	2814
Limitations in the evidence				
Risk of bias (based on 152 studies)	Participants: high (40) or unclear (45) risk in 85 studies (56%) Index test: high (6) or unclear (45) risk in 51 studies (34%) Reference standard: high (119) or unclear (18) risk in 137 studies (90%) Flow and timing: high (41) or unclear (69) risk in 110 studies (72%)			
Concerns about applicability (based on 152 studies)	Participants: high concerns in 45 studies (30%) Index test: high concerns in 47 studies (31%) Reference standard: high concerns in 139 studies (91%)			
Findings from studies reporting both sensitivity and specificity				
	Evaluations	Samples (SARS-CoV-2 cases)	Sensitivity (95% CI)	Specificity (95% CI)
Symptomatic*	109	50,574 (11,662)	73.0 (69.3 to 76.4)	99.1 (99.0 to 99.2)^a
Subgroup ≤ 7 days from symptom onset ^b *	30	15,323 (2408)	80.9 (76.9 to 84.4)	99.5 (99.3 to 99.6)
Subgroup: COVID-19 test centre	47	23,602 (4369)	82.8 (80.2 to 85.2)	99.1 (99.0 to 99.2)
Asymptomatic	50	40,956 (2641)	54.7 (47.7 to 61.6)	99.5 (99.4 to 99.6)
Subgroup: widely available testing*	26	31,904 (1758)	49.6 (42.1 to 57.1)	99.6 (99.5 to 99.7)
Subgroup: contacts*	16	7677 (703)	64.3 (54.6 to 73.0)	99.7 (99.5 to 99.8)
Any symptom status	Evaluations	SARS-CoV-2 cases	Sensitivity (95% CI)	

Subgroup: $\geq 10^7$ RNA copies/mL	21	608	98.4 (97.0 to 99.1)	-
Subgroup: $\geq 10^6$ to $< 10^7$ RNA copies/mL	28	597	94.0 (89.8 to 96.6)	-
Subgroup: $\geq 10^5$ to $< 10^6$ RNA copies/mL	31	686	70.9 (57.4 to 81.5)	-
Subgroup: $\geq 10^4$ to $< 10^5$ RNA copies/mL	24	582	36.7 (24.7 to 50.5)	-
Subgroup: $< 10^4$ RNA copies/mL	24	825	7.5 (3.8 to 14.3)	-

Symptomatic participants: average sensitivity and specificity (and 95% CIs) applied to a hypothetical cohort of 1000 patients where 50, 100 and 200 have COVID-19 infection

	Prevalence	TP (95% CI)	FP (95% CI)	FN (95% CI)	TN (95% CI)	PPV ^c	1 - NPV ^d
Symptomatic (any symptomatic)	5%	37 (35 to 50)	9 (8 to 10)	14 (1 to 15)	941 (940 to 942)	81%	1.4%
	10%	73 (69 to 99)	8 (7 to 9)	27 (1 to 31)	892 (891 to 893)	90%	2.9%
	20%	146 (139 to 198)	7 (6 to 8)	54 (2 to 61)	793 (792 to 794)	95%	6.4%
Symptomatic (week 1 after symptom onset)	5%	40 (38 to 42)	5 (4 to 7)	10 (8 to 12)	945 (943 to 946)	89%	1.0%
	10%	81 (77 to 84)	5 (4 to 6)	19 (16 to 23)	896 (894 to 896)	95%	2.1%
	20%	162 (154 to 169)	4 (3 to 6)	38 (31 to 46)	796 (794 to 797)	98%	4.6%

Asymptomatic participants: average sensitivity and specificity (and 95% CIs) applied to a hypothetical cohort of 10,000 patients where 50, 100 and 200 have COVID-19 infection

Asymptomatic (widely available testing)	0.5%	25 (21 to 29)	40 (30 to 50)	25 (21 to 29)	9910 (9900 to 9920)	38%	0.3%
	1%	50 (42 to 57)	40 (30 to 50)	50 (43 to 58)	9860 (9851 to 9870)	52%	0.5%
	2%	99 (84 to 114)	39 (29 to 49)	101 (86 to 116)	9760 (9751 to 9770)	72%	1.0%
Asymptomatic (contacts)	0.5%	32 (27 to 50)	30 (20 to 50)	18 (14 to 23)	9920 (9900 to 9930)	52%	0.2%

1%	64 (55 to 73)	30 (20 to 50)	36 (27 to 45)	9870 (9850 to 9880)	68%	0.4%
2%	129 (109 to 146)	29 (20 to 49)	71 (54 to 91)	9770 (9751 to 9780)	81%	0.7%

1 – NPV: 1 – negative predictive value (the percentage of people with negative results who are infected); **Ag:** antigen; **CI:** confidence interval; **Ct:** cycle threshold; **FN:** false negative; **FP:** false positive; **PPV:** positive predictive value (the percentage of people with positive results who are infected); PCR: reverse transcription polymerase chain reaction; **TMA:** transcription-mediated amplification; **TN:** true negative; **TP:** true positive

* denotes data used for hypothetical cohort scenarios

^aExcludes outlier with 8% specificity in 13 throat saliva or throat wash samples.

^bResults reported are for studies reporting both sensitivity and specificity; including sensitivity-only cohorts (total n = 72), sensitivity was 82.2% (95% confidence interval 79.2% to 85.0%) in 5640 PCR+ve samples.

^cPPV (positive predictive value) defined as the percentage of positive rapid test results that are truly positive according to the reference standard diagnosis.

^d1-NPV (negative predictive value), where NPV is defined as the percentage of negative rapid test results that are truly negative according to the reference standard diagnosis.

BACKGROUND

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resulting COVID-19 pandemic present important diagnostic evaluation challenges. These range from: understanding the value of signs and symptoms in predicting possible infection; assessing whether existing biochemical and imaging tests can identify infection or people needing critical care; and evaluating whether *in vitro* diagnostic tests can accurately identify and rule out current SARS-CoV-2 infection, and identify those with past infection, with or without immunity.

We are creating and maintaining a suite of living systematic reviews to cover the roles of tests and patient characteristics in the diagnosis of COVID-19. This review is the second update of a review summarising evidence of the accuracy of rapid antigen tests that are suitable for use at the point of care. The review was first published in August 2020 (Dinnes 2020), and updated in March 2021 (Dinnes 2021), and originally investigated both rapid antigen tests and rapid molecular tests for diagnosis of SARS-CoV-2. This review focuses solely on rapid antigen tests. Rapid tests may have potential to be used as alternatives to standard laboratory-based molecular assays, such as reverse transcription polymerase chain reaction (RT-PCR) assays, that are relied on for identifying current infection, or may be used where no testing is currently done. If sufficiently accurate, point-of-care tests have the potential to greatly expand access and speed of testing. In turn, if accurate, they may have greater impact on public health than laboratory-based molecular methods as they are less expensive, provide results more quickly and do not require the same technical expertise and laboratory capacity. These tests can be undertaken locally, avoiding the need for centralised testing facilities that rarely meet the needs of patients, caregivers, health workers and society as a whole, especially in low- and middle-income countries. As these are rapid tests, their results can be returned within the same clinical encounter, facilitating timely decisions concerning the need for isolation and contact tracing activities.

Target condition being diagnosed

COVID-19 is the disease caused by infection with the SARS-CoV-2 virus. The key target conditions for this suite of reviews are current SARS-CoV-2 infection, current COVID-19 disease, and past SARS-CoV-2 infection. The tests included in this review concern the identification of current infection, as defined by reference standard methods of diagnosis, including molecular assays such as reverse transcription polymerase chain reaction (RT-PCR), or internationally recognized clinical guidelines for diagnosis of SARS-CoV-2. In the context of test evaluation, and throughout this review, we use the term 'reference standard' to denote the best available method (test or tests) for diagnosing the target condition, as opposed to other uses of the term in diagnostic virology (such as reference methods or reference materials).

For current infection, the severity of the disease is of ultimate importance for patient outcomes. Rapid testing does not establish severity of disease, and for this review we consider the role of point-of-care antigen tests for detecting SARS-CoV-2 infection of any severity, distinguishing only between symptomatic and asymptomatic infection. In addition, the increasing occurrence of SARS-CoV-2 variants of concern since the last published iteration of this review could have some as yet unknown impact on the accuracy of rapid diagnostic tests (RDTs), particularly if mutations

take place in the nucleocapsid gene ('N' gene), which encodes the virus nucleoprotein and is the main target of the majority of antigen-based RDTs (FIND 2022b).

COVID-19 public health interventions focus on increasing uptake of COVID-19 vaccination and on reducing disease transmission. Immunity from infection varies between individuals, even in those vaccinated or who have had a prior COVID-19 infection and immunity also wanes over time, therefore early identification of infection remains an important public health goal. Government policies in regard to testing, self-isolation and quarantine have changed over the course of the pandemic, however, as a general principle, people with symptoms who meet national criteria for COVID-19 testing are reasonably expected to self-isolate to avoid infecting others while awaiting the result from a PCR test. Contacts of confirmed cases have been similarly considered to have a high enough risk of being infectious to ask them to quarantine for 7 to 10 days. The UK and USA introduced policies based on rapid tests, both to allow 'early' release from self-isolation for those with confirmed SARS-CoV-2 infection and daily rapid antigen testing for fully vaccinated contacts of confirmed cases, with self-isolation only required following a positive antigen test result (UK HSA 2021a). Assessing the risk of an individual being infectious in asymptomatic screening is difficult, however, as there is no reference standard test for being 'infectious'. Using RT-PCR status as a reference standard (as is done for the target condition of 'infection') will ensure that infectious people are not missed, but because RT-PCR continues to detect viral ribonucleic acid (RNA) days and weeks after the onset of infection it will wrongly classify some infected people as infectious.

A reference standard that has been proposed for establishing infectiousness is viral culture. Viral culture is technically complex and requires high levels of biosafety containment, such that it is not suitable for routine use. Furthermore it can be unreliable (the failure to culture virus potentially being a result of the culture technique and not an indicator of non-infectiousness). For example, in Smith 2021, viral culture failed in samples from 8 of 51 (16%) newly infected adults.

Alternatively, a value of the cycle threshold (Ct value) from RT-PCR results to group individuals above or below a particular value as more or less likely to be infectious has become commonplace (Petersen 2021; UK DHSC 2021b; WHO 2020b). The suitability of RT-PCR Ct values (also known as quantification cycle (Cq) or crossing point (Cp) values) as a proxy indicator of infectiousness is limited for a number of reasons, however. Firstly, the relationship between Ct values and viral load varies between machines and laboratories and RT-PCR assays, even where the same genetic targets are used (Binnicker 2020), and is further affected by sample collection and processing (IDSA 2021), so that comparison at fixed Ct values is unlikely to be comparable across studies. Recent work by Evans and colleagues converting Ct values into direct quantitative values of viral load (viral copies per cell) demonstrated inter-laboratory variation of more than 1000-fold in copies/mL for a given Ct value measuring the same sample (Evans 2021). Secondly, although conversion from Ct values to RNA copies/mL allows for a fairer comparison in results between studies when done correctly (i.e. using a quantitative PCR calibrated to a robust standard curve derived from certified reference material), the use of different and potentially suboptimal methods of calculating viral load from Ct values has potential to introduce variability in results (Evans 2021). Thirdly, the inverse relationship between viral load and risk

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of infecting others is a continuum of risk without there being a meaningful cut-point either in terms of Ct or genomic copies/mL. Studies have evidenced successful viral culture from samples with Ct values as high as 35 (Singanayagam 2020), and transmission of infection from index cases with higher Ct values (Lee 2021; Marks 2021; Tian 2021). A linked data analysis using available empirical data suggests a non-negligible risk of onward transmission of infection from cases with higher Ct values (Deeks 2022). Finally, even the most precise estimation of viral load does not overcome the inability of a single test to identify whether individuals with low viral loads are at the onset of infection and therefore likely to be infectious for a period of time or are recovering from infection and have declining viral load.

Tracking contacts of SARS-CoV-2 cases for evidence of infection provides the best insight into the dynamics of viral transmission, however this requires longitudinal follow-up and predictive modelling to take into account host, agent and environmental factors, all of which influence risk of transmission. This contrasts with the diagnostic test accuracy paradigm which can only determine if individuals are infected at a single point in time.

Because of the lack of a suitable reference standard for detection of 'infectiousness', this review only focuses on the target condition of 'infection' for applications of tests in both symptomatic and asymptomatic individuals. Although the presence of COVID-19 can be defined clinically (e.g. for individuals with negative RT-PCR results), the primary reference standard for presence or absence of SARS-CoV-2 infection is RT-PCR. While acknowledging the potential for between-study variability in viral load associated with Ct values in particular, we report results in subgroups by Ct value and by RNA copies/mL, and continue to advise caution in interpretation. Given the current state of the scientific knowledge we do not consider it appropriate to consider these as groups that are 'infectious' or 'not infectious'.

RT-PCR carries a very small risk of false positive results for infection and a higher risk of false negative results. False positive results may result from failures in sampling or laboratory protocols (e.g. mislabelling), contamination during sampling or processing, or low-level reactions during PCR (Healy 2020; Mayers 2020). As for the previous iteration of this review we consider the upper bound on the possible false positive rate of RT-PCR of less than 0.077%. This estimate is based on population prevalence surveys showing RT-PCR positivity rates (comprising both true positive and false positive results) of 0.44% in August 2020 (95% credible interval 0.22% to 0.76%; ONS 2020), and 0.077% (95% credible interval 0.065%, 0.092%) in the React-1 study from June to July 2020 (Riley 2020). False negative rates have been estimated by looking at individuals with symptoms who initially test negative, but test positive on a subsequent test. These rates have been estimated to be as high as 20% to 30% in the first week of symptom onset (Arevalo-Rodriguez 2020a; Kucirka 2020; Yang 2020a; Zhao 2020). Including probable COVID-19 cases within the target condition, as defined by internationally recognized clinical guidelines for diagnosis of SARS-CoV-2, will partially mitigate these missed cases.

Index test(s)

Previous iterations of this living review included two types of test that could be deployed at the point of care: rapid antigen tests and rapid molecular tests (see Appendix 1 for the definition of 'point of care' that has been used in these reviews). Given

the widespread international interest in using rapid antigen tests, and the many different settings in which they can be deployed compared to rapid molecular tests, this review update focuses only on antigen detection tests (referred to here as rapid diagnostic tests or RDTs), which can be used at the point of care or in non-healthcare settings such as in the home. In this iteration of the review we include evaluations of single applications of a test (i.e. used for diagnostic purposes in symptomatic or asymptomatic populations) and evaluations of serial testing strategies in asymptomatic populations (i.e. repeated applications of a test for earlier detection of infection). We intend to update the review of rapid molecular tests separately at a later date.

Antigen RDTs (and rapid molecular assays) typically use the same upper respiratory-tract samples obtained for laboratory-based RT-PCR, that is, nasopharyngeal or combined naso- and oropharyngeal samples, although many companies have test kits for use with anterior nasal or nasal mid-turbinate samples. The majority of RDTs are lateral flow immunoassays (LFAs), which are disposable devices, usually in the form of plastic cassettes akin to an over-the-counter pregnancy test. SARS-CoV-2 antigens, most commonly the nucleoprotein, are captured by dedicated and labelled antibodies, typically colloidal gold- or fluorescent-labelled, although other assay formats are also available. The liquid sample is absorbed via passive capillary action, and the presence of the target antigen is indicated within 15 to 30 min either by visible lines appearing on the test strip, or through fluorescence, which can be detected using an immunofluorescence analyser. Microfluidic analytical devices are also being developed for SARS-CoV-2, typically using reader devices for test interpretation. These devices are based on the lateral flow format, using active capillary action to guide liquid samples along the test strip to the desired outlets where the chemical or biochemical reactions take place (Jiang 2021). The assays are intended to detect the target antigen at lower concentrations compared to conventional LFAs (Noel 2021).

Although antigen RDTs have been shown to be on average less sensitive than rapid molecular tests (Dinnes 2021), there are considerably fewer logistical and economic barriers to their use. This has led to widespread international adoption of RDTs, and prolific industry activity to develop more accurate tests. The Foundation for Innovative Diagnostics (FIND) and Johns Hopkins Centre for Health Security have maintained online lists of available tests for SARS-CoV-2 (FIND 2022a). At the time of writing (20 December 2021), FIND listed 321 commercially available rapid antigen tests, almost all with known regulatory approval. These numbers are a considerable increase on the 92 with regulatory approval at the time of writing the last review iteration (5 January 2021), and the 21 with regulatory approval at the time of our original review (19 July 2020). This classification was based on the information provided to FIND by the test manufacturers and does not necessarily mean that these tests meet the criteria for point-of-care tests that we have specified for this review.

For this iteration of the review, we continue to only include evaluations of commercially produced tests. All commercially produced assays are supplied with a specific product code, product inserts or instructions for use (IFU) sheets that document the intended use of the test, sample storage and preparation and testing procedures.

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Clinical pathway

Patients may be tested for SARS-CoV-2 when they present with symptoms, have had known exposure to a confirmed case, or in a screening context, with no known exposure to SARS-CoV-2. The standard approach to diagnosis of SARS-CoV-2 infection is through laboratory-based testing of swab samples taken from the upper respiratory (e.g. nasopharynx, oropharynx) or lower respiratory tract (e.g. bronchoalveolar lavage or sputum) with RT-PCR. RT-PCR is the primary method for detecting infection during the acute phase of the illness while the virus is still present. Both the WHO and the China CDC (National Health Commission of the People's Republic of China) have produced case definitions for COVID-19 that include the presence of convincing clinical evidence (some including positive serology tests) when RT-PCR is negative (Appendix 2).

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 2021). However, the Cochrane Review of signs and symptoms found that the majority of individual signs and symptoms have very poor diagnostic accuracy; neither absence nor presence of signs or symptoms were accurate enough to rule in or rule out disease (Struyf 2021). The review suggested that multivariable prediction models combining symptoms with other information such as contact or travel history, age, gender, and a local recent case detection rate, could reach sensitivities as high as 90%, however further research is needed to identify the optimal combination of variables (Struyf 2021). With reports of changing symptom profiles by age (Canas 2021), and by vaccination status (Zoe COVID Study 2021), rapid testing of symptomatic individuals is likely to remain a vital tool in managing the COVID-19 pandemic (Crozier 2021). Where people are asymptomatic but are being tested as part of screening (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.

Role of index test(s)

For most settings in which testing for acute SARS-CoV-2 infection in symptomatic individuals takes place, results of molecular laboratory-based RT-PCR tests are unlikely to be available within a single clinical encounter. Point-of-care tests potentially have a role either as a replacement for RT-PCR (if sufficiently accurate), or as a means of triaging and rapid management (isolation or treatment, or both), with RT-PCR testing for those with negative rapid test results (CDC 2021; WHO 2020a). Obtaining quick results within a single healthcare visit will allow faster decisions about isolation and healthcare interventions for those with positive test results, and allow contact tracing to begin in a more timely manner. Modelling studies suggest contact tracing is most effective if it starts within 24 hours of case detection, with delays in testing (e.g. due to laboratory turnaround time for reporting PCR results) leading to reductions in the proportion of onward transmissions per index case that can be prevented by track and trace (Kretzschmar 2020).

If sufficiently accurate, negative rapid test results in symptomatic patients could allow faster return to work or school after symptom resolution, therefore conferring important economic and educational implications. Negative results also allow immediate consideration of other causes of symptoms, which may be time-sensitive, for example bacterial pneumonia or thromboembolism.

For asymptomatic individuals, if accurate, rapid tests may also be considered for screening at-risk (exposed) populations, for example in hospital workers or in local outbreaks, or for targeted screening with single test application at airports or for border entry, to allow entry to large public gatherings (Revollo 2021), or screening students as a risk-reduction strategy (Ferguson 2021). Because rapid antigen tests can easily be delivered at scale, they have also been deployed for mass screening purposes as piloted in Slovakia (Frnda 2021), and in Liverpool, UK (Garcia-Finana 2021). Community mass antigen testing for SARS-CoV-2 is now used internationally, under national (e.g. UK (Iacobucci 2020), or Slovakia (Frnda 2021)), or regional policies (e.g. USA (Prince-Guerra 2021), or Spain (Pena 2021), amongst others). Frequent repeated use of antigen tests in asymptomatic individuals with no known exposure to identify COVID-19 cases has also been proposed in a number of modelling studies (Larremore 2020), but field trial evaluations to confirm the suggested promising results remain scarce (e.g. Young 2021), and are not without criticism (Gurdasani 2021). Nevertheless, UK residents, including secondary school pupils, are recommended to use a freely available (at the time of writing) rapid antigen test twice per week (NHS 2021; UK Department for Education 2022), with daily contact testing trials completed (UK DHSC 2021a), or recently published (Young 2021).

Alternative test(s)

This review is one of eight that cover the range of tests and clinical characteristics being considered in the management of COVID-19 (Deeks 2020a; McInnes 2020; Leeflang 2021), five of which have already been published (Deeks 2020b; Islam 2021; Stegeman 2020; Struyf 2021), including the first two iterations of this review (Dinnes 2020; Dinnes 2021). Full details of the alternative tests and evidence of their accuracy is summarized in these reviews. The SARS-CoV-2-specific biomarker tests that might be considered as alternatives to point-of-care tests are considered here.

Rapid point-of-care molecular assays

Molecular-based tests to detect viral RNA have historically been laboratory-based assays using RT-PCR technology (see below). In recent years, automated, single-step RT-PCR methods have been developed, as well as other nucleic acid amplification methods, such as isothermal amplification, that do not require the sophisticated thermo cycling involved in RT-PCR (Green 2020). These technological advances have allowed molecular technologies to be developed that are suitable for use in a point-of-care context (Kozel 2017), however they require small portable machines, are more expensive and many take longer to produce results than antigen tests, although recent advances in the turnaround time have been made. For logistical and economic reasons therefore, the use cases for the majority of rapid molecular assays are quite different to point-of-care antigen tests and so they will now be included in a separate review in this series of living reviews.

Laboratory-based molecular tests

PCR methods are routinely used for detection of viral RNA (Behera 2021). SARS-CoV-2-specific reagents for RT-PCR detection of SARS-CoV-2 were produced soon after the viral RNA sequence was published (Corman 2020). Testing is undertaken in central laboratories and can be very labour-intensive, with several points along the path of performing a single test where errors may occur, although some automation of parts of the process is possible. The amplification process requires thermal cycling equipment to allow multiple temperature changes within a cycle, with cycles repeated up to 40 times until viral DNA is detected (Carter 2020). Although the amplification process for RT-PCR can be completed in a relatively short timeframe, the stages of extraction, sample processing and data management (including reporting) mean that test results are typically only available in 24 to 48 hours. Where testing is undertaken in a centralized laboratory, transport increases this time further. The time to result for fully automated RT-PCR assays is shorter than for manual RT-PCR, however most assays still require sample preparation steps that make them unsuitable for use at the point of care.

Other nucleic acid amplification methods, including loop-mediated isothermal amplification (LAMP), or CRISPR-based nucleic acid detection methods, that allow amplification at a constant temperature are now commercially available (Chen 2020), and are the subject of a separate review in this series that is currently under preparation (Deeks 2020a).

Laboratory-based antigen detection tests

Antigen detection tests can also be performed in the laboratory, using automated or semi-automated enzyme immunoassays (EIA) like enzyme-linked immunosorbent assays (ELISA) or more advanced chemiluminescence immunoassays (CLIAs). Because of the limitations in detecting the SARS-CoV-2 virus in plasma or serum, antigen detection assays are primarily used with respiratory samples (Lai 2021).

Rationale

It is essential to understand the clinical accuracy of tests and clinical features to identify the best way they can be used in different settings to develop effective diagnostic and management pathways for SARS-CoV-2 infection and disease. The suite of Cochrane living systematic reviews summarizes evidence on the clinical accuracy of different tests and diagnostic features. Estimates of accuracy from these reviews will help inform diagnosis, screening, isolation, and patient-management decisions.

Summary of the previous version of the review

The first iteration of this review (Dinnes 2020), included five studies that evaluated five antigen detection tests (four commercial and one in-house). We did not find any studies at low risk of bias and had concerns about applicability of results across all studies. The average sensitivity was 56.2% (95% confidence interval (CI) 29.5 to 79.8%) and average specificity 99.5% (95% CI 98.1% to 99.9%), based on 943 samples, 596 with confirmed SARS-CoV-2. Data for individual antigen tests were limited with no more than two studies for any test.

For the subsequent update of the review (Dinnes 2021, published in March 2021), we restricted inclusion to evaluations of commercially produced tests. We included 48 studies that reported 58

evaluations of 16 different commercially produced RDTs. We did not judge any study at low risk of bias, although in 23% (11/48) of studies the only bias present was that a single negative RT-PCR was used to confirm absence of SARS-CoV-2 infection rather than the preferred two negative tests. All studies raised concerns regarding the applicability of their results, but similarly, in 25% (12/48) of studies the only concern was the reliance on only PCR to identify SARS-CoV-2 cases.

Assay specificities were consistently high (overall summary specificity 99.6%, 95% CI 99.0% to 99.8%), however estimates of sensitivity varied considerably between studies and according to test brand. In particular we identified differences in sensitivity between symptomatic (72.0%, 95% CI 63.7% to 79.0%; 37 evaluations; 15,530 samples, 4410 cases) and asymptomatic participants (58.1%, 95% CI 40.2% to 74.1%; 12 evaluations; 1581 samples, 295 cases), and sensitivity was on average higher in the first week after symptom onset (78.3%, 95% CI 71.1% to 84.1%; 26 evaluations; 5769 samples, 2320 cases) compared to the second week of symptoms (51.0%, 95% CI 40.8% to 61.0%; 22 evaluations; 935 samples, 692 cases). Sensitivity was high in those with PCR cycle threshold (Ct) values less than 25 (94.5%, 95% CI 91.0% to 96.7%; 36 evaluations; 2613 cases) compared to those with Ct values above 25 (40.7%, 95% CI 31.8% to 50.3%; 36 evaluations; 2632 cases). Using data from evaluations that were compliant with manufacturer instructions for use (IFU), summary sensitivities ranged from 34.1% (95% CI 29.7% to 38.8%; Coris Bioconcept) to 88.1% (95% CI 84.2% to 91.1%; SD Biosensor STANDARD Q). Only the STANDARD Q assay met the WHO acceptable criterion for sensitivity based on summary results across several studies.

Changes in the evidence base since the previous version

There has been a considerable increase in the number of available evaluations of antigen tests, in both symptomatic and asymptomatic populations. More studies report results for direct swab testing using nasal swab samples which are considered to be easier and more comfortable to collect than nasopharyngeal swabs. More direct comparisons of the accuracy of different test brands and, to a lesser extent, according to sampling site or type of test operator are now available. This review considers the available evidence in relevant population groups and settings according to test brand and compliance with manufacturer IFUs. We also aimed to consider any impact on test accuracy from infection with variants of concern or from vaccination status, although we anticipated that the influence from these factors may not yet be reflected in the evidence base. We used the WHO's priority target product profiles for COVID-19 diagnostics (i.e. acceptable performance criterion of sensitivity of 80% or higher and specificity 97% or higher, or desirable criterion of 90% sensitivity or higher and 99% specificity or higher; WHO 2020b), as a benchmark against which to consider test performance.

We will update this review as often as is feasible to ensure that it provides current evidence about the accuracy of point-of-care tests.

This review follows a generic protocol that covers six Cochrane COVID-19 diagnostic test accuracy (DTA) reviews (Deeks 2020a). The Background and Methods sections of this review therefore use some text that was originally published in the protocol (Deeks 2020a), in the previous iteration of this review (Dinnes 2020; Dinnes 2021), and text that overlaps some of our other reviews (Deeks 2020b; Struyf 2021).

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

OBJECTIVES

To assess the diagnostic accuracy of rapid point-of-care antigen tests to for diagnosis of SARS-CoV-2 infection. We consider accuracy separately in symptomatic and asymptomatic population groups.

Secondary objectives

Within each group by symptom status we explored the effect of study setting and for asymptomatic populations, epidemiological exposure to SARS-CoV-2 (i.e. testing of contacts of confirmed cases compared to widely available testing of asymptomatic individuals with no requirement to meet pre-set criteria for testing).

Additional sources of heterogeneity investigated (either by stratified analysis or meta-regression) included assay format, duration of symptoms, viral load and participant age group (adults or children). We also aimed to investigate accuracy according to SARS-CoV-2 variant and participant vaccination status, however insufficient evidence was identified. Although the reference standard used can influence accuracy, we anticipated that as in previous iterations of this review, all studies would rely on RT-PCR.

We investigated adherence to manufacturers' IFUs in sensitivity analyses.

METHODS

Criteria for considering studies for this review

Types of studies

We applied broad eligibility criteria to include all patient groups (that is, if patient population was unclear, we included the study) and all variations of a test.

We included studies of all designs that produce estimates of test accuracy or provide data from which we can compute estimates, including the following.

- Single-group studies, which recruit participants before disease status has been ascertained.
- Multi-group studies, where people with and without the target condition are recruited separately (often referred to as two-gate or diagnostic case-control studies)
- Studies restricted to participants confirmed to either have (or to have had) the target condition (to estimate sensitivity) or confirmed not to have (or have had) the target condition (to estimate specificity). These types of studies may be excluded in future review updates.
- Studies based on either participants or samples

We excluded studies from which we could not extract data to compute either sensitivity or specificity.

We carefully considered the limitations of different study designs in the methodological quality assessment and analyses.

We included studies reported in published journal papers, as preprints, and publicly available reports from independent bodies.

Participants

We included studies recruiting people presenting with suspicion of current SARS-CoV-2 infection or those recruiting populations where

tests were used to screen for infection (for example, contact tracing or community screening).

We also included studies that recruited people known to have SARS-CoV-2 infection and known not to have SARS-CoV-2 infection (i.e. cases only or multi-group studies).

We excluded small studies with fewer than 10 samples or participants. Although the size threshold of 10 is arbitrary, such small studies are likely to give unreliable estimates of sensitivity or specificity and may be biased.

Index tests

We included studies evaluating any rapid antigen-detection test for diagnosis of SARS-CoV-2, if it met the criteria outlined in Appendix 1. In brief, this includes:

- minimal equipment required;
- minimal sample preparation and biosafety considerations;
- results available within two hours of sample collection; and
- commercially produced (with test name and manufacturer or distributor documented).

Any respiratory sample type was eligible. Strategies based on multiple applications of a test were also eligible for inclusion.

We excluded studies that evaluated rapid molecular-based tests from this review iteration.

Target conditions

The target condition was current SARS-CoV-2 infection (either symptomatic or asymptomatic). We also refer to SARS-CoV-2 infection as 'COVID-19 infection', particularly in the Plain language summary and [Summary of findings 1](#).

Reference standards

We originally anticipated that studies would use a range of reference standards to define both the presence and absence of SARS-CoV-2 infection, however we have found for both previous iterations of this review that all studies used laboratory-based RT-PCR assays to confirm the presence of SARS-CoV-2 infection and almost all also used RT-PCR to confirm absence of infection (a very small proportion using pre-pandemic respiratory samples). For this iteration of the review we therefore considered the use of any molecular assay as a suitable reference standard for confirmation of the presence or absence of SARS-CoV-2. Studies using pre-pandemic samples as non-SARS-CoV-2 cases were also eligible.

Search methods for identification of studies

The previous iteration of this review included records from electronic searches (up to 30 September 2020) and additional online resources (manually checked 16 November 2020). Search methods for prior iterations of the review are documented in Appendix 3. This section documents additional searches undertaken for the current iteration of this living review up to 8 March 2021.

Electronic searches

COVID-19 Open Access Project (COAP) living evidence database from the University of Bern

We used the COVID-19 Open Access Project living evidence database from the Institute of Social and Preventive Medicine (ISPM) at the University of Bern ([COVID-19 Open Access Project 2021](#)). The last feed obtained for this review was 8 March 2021. 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 ISPM website are described here (ispmbern.github.io/covid-19/living-review/collectingdata.html). See Appendix 3.

Since 25 May 2020 we have used review-specific artificial intelligence text analysis to classify retrieved records based on their title and abstract information, for relevant and irrelevant documents (documented in Appendix 4).

Searching other resources

We contacted or accessed the websites of independent research groups undertaking test evaluations (for example, UK Public Health England (PHE), the Société Française de Microbiologie (SFM), the Dutch National Institute for Public Health and the Environment (RIVM)) and studies co-ordinated by FIND (finddx.org/covid-19/sarscov2-eval) and accessed the Diagnostics Global Health listing of manufacturer-independent evaluations of antigen detecting rapid diagnostic tests (Ag-RDTs) for SARS-CoV-2 (diagnosticsglobalhealth.org). We last accessed these additional resources on 30 April 2021.

We appeal to researchers to supply details of additional published or unpublished studies at the following email address, which we will consider for inclusion in future updates (coviddta@contacts.bham.ac.uk).

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 following the application of artificial intelligence text analysis (described in [Electronic searches](#)). Two review authors independently screened studies in [Covidence](#). A third, senior review author resolved any disagreements.

We obtained the full texts for all studies flagged as potentially eligible. Two review authors independently screened the full texts; any disagreements on study inclusion were resolved through discussion with a third review author.

Up to September 2020 screening was conducted across all Cochrane COVID-19 DTA biomarker reviews (molecular, antigen or antibody tests), 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 to different reviews.

Data extraction and management

One review author extracted the characteristics of each study, which a second review author checked. Items that we extracted are listed in Appendix 5.

Both review authors independently performed data extraction of 2x2 contingency tables of the number of true positives, false positives, false negatives and true negatives. They resolved disagreements by discussion. Where possible, we separately extracted data according to symptom status (symptomatic, asymptomatic, mixed symptom status or not reported), viral load as defined per study (either in subgroups by Ct values or RNA copies/mL), time post-symptom onset (week one versus week two), and for children (≤ 16 years or ≤ 18 years) and adults. We extracted information about accuracy according to SARS-CoV-2 variant where reported, however we did not identify any information about participant vaccination status in the included studies. For categorization by symptom status, we classed studies reporting at least 75% of participants as symptomatic (or asymptomatic) as 'mainly symptomatic' (or 'mainly asymptomatic'), we considered studies with less than 75% symptomatic participants to report 'mixed' groups along with those that reported recruiting both symptomatic and asymptomatic participants but did not provide the percentages in each group. We considered studies that provided no information as to the symptom status of included participants 'not reported'. We also coded evaluations according to compliance with manufacturer IFUs. We based coding on three aspects of testing:

- sample type (use of any sample not explicitly mentioned on the IFU scored 'No', otherwise scored 'Yes'),
- for evaluations using samples that had been stored in viral transport medium (VTM) only (scored 'Yes' if specific instructions were provided and conditions were met; scored 'Unclear' if no instructions for use of samples in VTM were provided in the IFU; scored 'No' if instructions provided were not followed); and
- timing between sample collection and testing (scored 'Yes' only if all tests were carried out within the specified time period, e.g. immediate on-site testing, or for testing in laboratories if all tests reported to have been carried out within the specified time period; scored 'Unclear' if time frame for testing was not reported and 'No' if any testing was carried out beyond the maximum stipulated timeframe).

We encourage study authors to contact us regarding missing details on the included studies (coviddta@contacts.bham.ac.uk).

Assessment of methodological quality

Two review authors independently assessed risk of bias and applicability concerns using the QUADAS-2 (Quality Assessment tool for Diagnostic Accuracy Studies) checklist tailored to this review (Appendix 6; [Whiting 2011](#)). The two review authors resolved any disagreements by discussion.

Ideally, studies examining the use of tests in symptomatic people should prospectively recruit a representative sample of participants presenting with signs and symptoms of COVID-19, either in community or primary care settings or in a hospital setting, and they should clearly record the time of testing after the onset of symptoms. Studies in asymptomatic people at risk of infection should document time from exposure. Studies applying tests in a

screening setting should document eligibility criteria for screening, particularly if a targeted approach is used and should take care to record any previous confirmed or suspected SARS-CoV-2 infection or any relevant epidemiological exposures. Studies should perform tests in their intended use setting, using appropriate samples with or without VTM and within the time period following specimen collection as indicated in the IFU document. Tests should be interpreted blinded to the final diagnosis (presence or absence of SARS-CoV-2). The reference standard diagnosis should be blinded to the result of the rapid test, and should not incorporate the result of the rapid test. We considered the use of a molecular assay to define the presence of SARS-CoV-2 infection to have a low risk of bias because a positive result can be taken to indicate the presence of infection, even if it does not reflect the time point in the course of infection. If the reference standard includes clinical diagnosis of COVID-19 for RT-PCR-negative patients, then established criteria should be used. Studies using pre-pandemic samples for estimating specificity have a low risk of bias because samples are from participants known not to have COVID-19. Those using contemporaneously collected samples have a higher risk of disease misclassification because of the inherent false negative rate of molecular tests such as RT-PCR. For absence of infection, at least two RT-PCR-negative tests are required to confirm the absence of infection for symptomatic participants but one negative RT-PCR was considered sufficient for asymptomatic participants. Data should be reported for all study participants, including those where the result of the rapid test was inconclusive, or participants in whom the final diagnosis of COVID-19 was uncertain. Studies should report whether results relate to participants (one sample per participant), or samples (multiple samples per participant).

Statistical analysis and data synthesis

Studies sometimes referred to ‘samples’ rather than ‘patients’, however we do not suspect that inclusion of multiple samples per study participant was a significant issue. For consistency of terminology throughout the review, we refer to results on a per-sample basis. If studies evaluated multiple tests in the same samples, we included them multiple times. We present estimates of sensitivity and specificity per study for each test brand using paired forest plots, and summarize results using average sensitivity and specificity in tables as appropriate. As heterogeneity is apparent in many analyses, these point estimates must be interpreted as the average of a distribution of values.

We estimated summary sensitivities and specificities with 95% confidence intervals (CI) using the bivariate model (Chu 2006; Reitsma 2005), via the *meqrlogit* command of *Stata*/SE 17.0. When few studies were available, we simplified models by first assuming no correlation between sensitivity and specificity estimates and secondly by setting near-zero variance estimates of the random effects to zero (Takwoingi 2017). In cases where there was only one study per test, we reported individual sensitivities and specificities with 95% CI constructed using the binomial ‘exact’ (Clopper-Pearson) method (Clopper 1934).

Where studies presented only estimates of sensitivity or of specificity, we fitted univariate, random-effects, logistic regression models. In a number of instances where there was 100% sensitivity or specificity for all evaluations or there were fewer than three studies with highly similar sensitivity or specificity, we computed estimates and 95% CIs by summing the counts of true positives, false positives, false negatives and true negatives across 2x2 tables.

These analyses are clearly marked in the tables. We present all estimates with 95% confidence intervals.

Where the same set of studies evaluated different symptom status, age, sample types, or test brands, on the same group of patients, we made direct comparisons using bivariate models that included indicator variables. Our ability to make formal comparisons between antigen assay brands was limited by the small number of studies making direct comparisons of the same tests.

Investigations of heterogeneity

We examined heterogeneity between studies by visually inspecting the forest plots of sensitivity and specificity. Where adequate data were available, we investigated heterogeneity related to symptom status, study setting, reporting of possible epidemiological exposure (asymptomatic contacts compared to any asymptomatic individual tested), time post-symptom onset or post-contact with a confirmed case, sample site, age, viral load, test brand, and assay format by including indicator variables in the random-effects logistic regression models. We obtained absolute differences in sensitivity or specificity and corresponding P values post-estimation by using the model parameters and the *nlcom* command in *Stata*. In instances where only one study was available per test or when tests were being directly compared following summing of counts of the 2x2 tables, we performed test comparison using the two-sample test of proportions.

Sensitivity analyses

We estimated overall summary sensitivities and specificities restricted to studies using single group designs. We also estimated summary sensitivities and specificities according to test brand and symptom status using only studies that were compliant to the IFU. We estimated sensitivity with and without studies that only evaluated samples with RT-PCR-confirmed SARS-CoV-2 (and thus did not estimate specificity). We performed the same analysis for specificity in studies that only evaluated RT-PCR-negative control samples.

Assessment of reporting bias

Because of uncertainty about the determinants of publication and other sources of reporting bias for diagnostic accuracy studies and the inadequacy of tests for detecting funnel plot asymmetry, we made no formal assessment of reporting bias.

Updating

We are aware of additional studies published since the electronic searches were conducted on 4 March 2021 and plan to update this review imminently. We have already conducted the next search to 14 October 2021.

RESULTS

Results of the search

We screened 3952 unique records (published or preprints) for inclusion in this review update and for the forthcoming update of the rapid point-of-care molecular tests review. Of 486 records selected for further assessment, we assessed 235 reports, 166 of which reported studies that were eligible for inclusion in this review

update. See [Figure 1](#) for the PRISMA flow diagram of search and eligibility results ([McInnes 2018](#)).

Figure 1. Study flow diagram

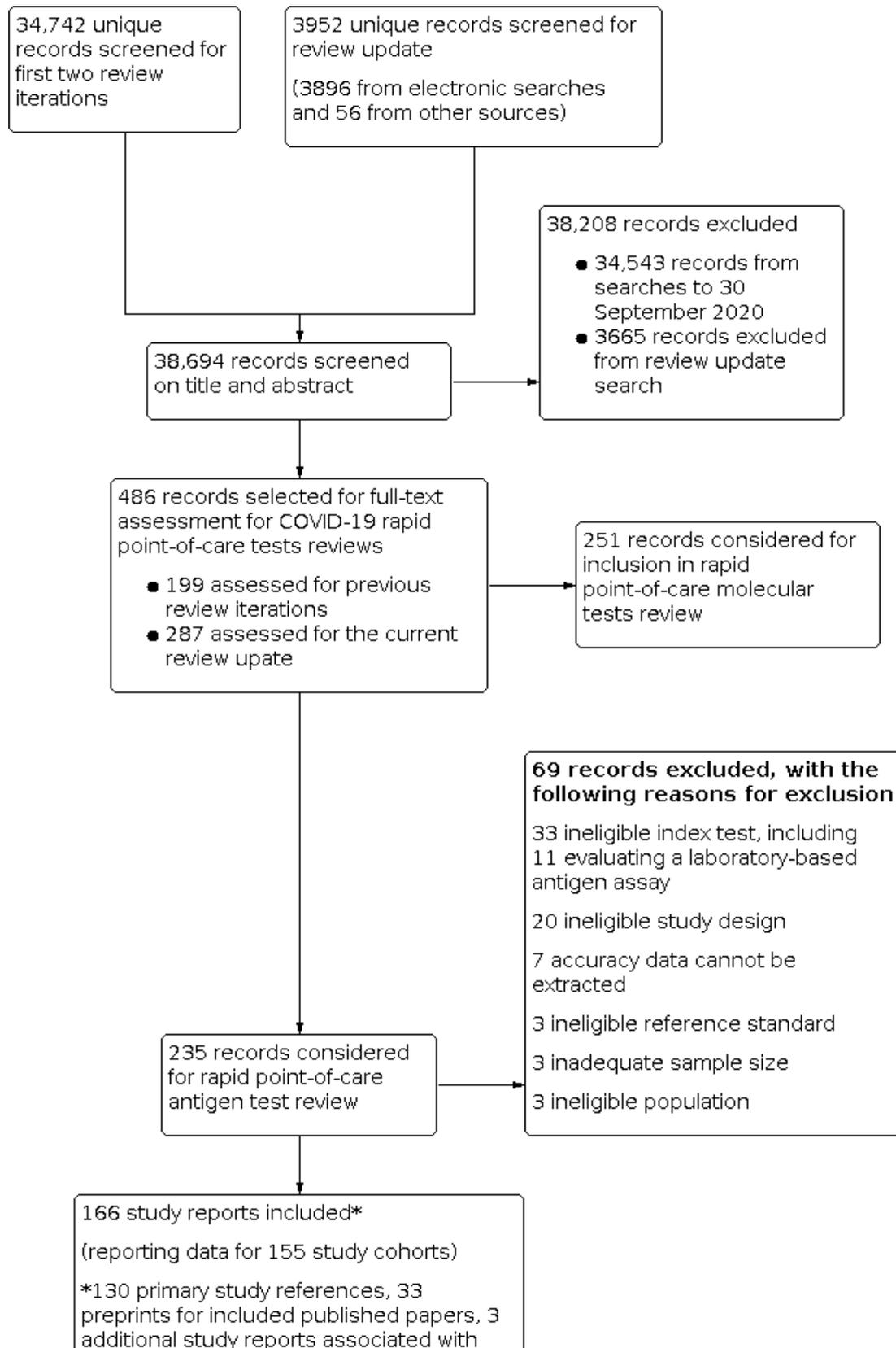


Figure 1. (Continued)

preprints for included published papers, 3 additional study reports associated with FIND evaluations

Of the 166 eligible study reports, 130 were primary study reports and 36 were secondary publications (for example preprints associated with published papers or journal papers associated with FIND evaluation reports). Of the 130 primary study reports, 87 were published journal papers, 24 were available only as preprints, and 19 were publicly available reports either from independent reference laboratories (one from Public Health England and two identified via the SMF) or were independent evaluations coordinated by FIND ($n = 16$). We excluded 69 publications that did not meet our inclusion criteria. Exclusions were mainly based on index test ($n = 33$, including 11 evaluating a laboratory-based antigen detection assay) or ineligible study designs ($n = 20$), for example, designs that did not allow estimation of test accuracy. One previously included preprint was excluded as we could not determine whether the test evaluated was the same as the subsequently commercially available assay (Diao 2020). The reasons for exclusion of all 69 publications are provided in [Characteristics of excluded studies](#).

For this iteration of the review we contacted the authors of 14 study reports for further information (Abdelrazik 2021; Abdulrahman 2020; Basso 2021 [A]; Caruana 2021 [A]; Faico-Filho 2021; Igloi 2021; Jakobsen 2021; Kriemler 2021; L'Huillier 2021; Schwob 2020(a); Torres 2021a; Torres 2021b; Bello-Chavolla 2021; Regev-Yochay 2021), and received replies in regard to eight studies.

The 130 primary study reports provide data for 155 separate cohorts of participants (henceforth referred to as 'studies'). Please note when naming studies, we use the letters [A], [B], [C] etc. in square brackets to indicate data on different tests evaluated in the same study and (a), (b), (c) to indicate data from different participant cohorts from the same study report. For example, the 16 included reports from FIND correspond to 22 'studies' because six reports separately provided data from more than one evaluation centre.

Of the 155 studies, 152 reported data for a single application of a rapid antigen test, three (Love 2021; Smith 2021; Winkel 2020), reported data for repeated testing of the same individuals over time, and one provided data for both a single test application and for repeat testing at a second testing time point (Kriemler 2021). The main results, Tables and Figures focus on the single test application studies, with results for repeated testing considered separately.

Description of included studies

The 152 studies reporting single test applications included a total of 100,462 unique samples, with 16,822 samples with RT-PCR-confirmed SARS-CoV-2 (some samples were analysed by more than one index test). Summary study characteristics are presented in [Table 1](#) with further details of study design and index test details in [Appendix 7](#) and [Appendix 8](#). Full details per study are provided in the [Characteristics of included studies](#).

The median sample size of the included studies is 326 (interquartile range (IQR) 149 to 744.5) and median number of SARS-CoV-2-confirmed samples included is 83.5 (IQR 45 to 135). Two-thirds

of the studies (101/152, 66%) were conducted in Europe, 17 in Asia, including one conducted in Russia (11%), 15 in North America (10%), 13 in South America (9%), and three in Africa. Two studies included samples from more than one country and in one, the country of sample origin was unclear.

Participant characteristics

Just over half of studies (78/152, 51%) were conducted at COVID-19 test centres (67, 44%) or at emergency or urgent care departments (11, 7%). Twenty-one studies were carried out in other hospital settings; including 11 in hospital inpatients, one including both inpatients and outpatients, and nine in patients, visitors, and staff. Six studies conducted screening in schools or universities, two reported screening of healthcare workers, and three conducted screening of the general population (defined as widely available testing with deliberate advertising to target community-wide populations). Four studies were conducted in shared living facilities (Dominguez Fernandez 2021; Kohmer 2021 [A]; PHE 2020; Toptan 2021(b)) and one in a quarantine centre as part of contact tracing (Shrestha 2020). Sixteen studies (11%) selected samples from those submitted to laboratories for routine RT-PCR testing often ($n = 7$) with limited detail of the participants providing the samples ('laboratory-based' studies). In six studies samples were included from multiple settings, and in the remaining 15 studies (10%) the selection of participants was not clearly reported.

Nearly half of the studies were conducted in symptomatic (55, 36%) or mainly symptomatic (18, 12%) populations. Seventeen studies (11%) were carried out in predominantly asymptomatic populations including any asymptomatic (9, 6%; Baro 2021 [A]; Ferguson 2021; Garcia-Finana 2021; Kriemler 2021; Okoye 2021; Pena 2021; Peto 2021(d); Pilarowski 2021; Rottenstreich 2021), asymptomatic contacts of confirmed cases (3, 2%; Fenollar 2020(b); Shrestha 2020; Torres 2021a), or mainly asymptomatic population (5, 3%; James 2021; Nalumansi 2020; Pollock 2021b; Pray 2021; Prince-Guerra 2021). The settings for testing asymptomatic people included: COVID-19 test centres ($n = 4$; Pilarowski 2021; Torres 2021a; Pollock 2021b; Prince-Guerra 2021), schools or universities ($n = 4$; Ferguson 2021; Kriemler 2021; Okoye 2021; Pray 2021), hospital settings ($n = 4$; including women admitted for delivery ($n = 1$; Rottenstreich 2021), healthcare worker screening ($n = 2$; James 2021; Peto 2021(d)), or participants not described ($n = 1$; Nalumansi 2020)), general public 'mass' screening ($n = 3$; Baro 2021 [A]; Garcia-Finana 2021; Pena 2021), a quarantine centre ($n = 1$; Shrestha 2020), or patient contacts for whom the setting for testing was not clearly reported ($n = 1$).

Forty-one studies were conducted in populations with mixed symptom status (27%), 20 of which did not report data separately for symptomatic and asymptomatic participants. Twenty-one studies did not provide information about symptom status for all included participants (13%): five included samples from a COVID-19 test centre (FIND 2021g; FIND 2021h; FIND 2021i; Gremmels 2021(b); Jaaskelainen 2021 [A]), two were conducted in shared living facilities (Kohmer 2021 [A]; Toptan 2021(b)), and in 14 the setting

for testing could not be derived, including seven that could be identified as laboratory-based studies.

One study deliberately included 23 RT-PCR positive swabs from people infected with the B.1.1.7 (Alpha) variant ([Pickering 2021\(c\) \[A\]](#); [Pickering 2021\(c\) \[B\]](#)). No effect on test accuracy was observed however sample numbers were small. This was the only study to consider the effect of SARS-CoV-2 variant on sensitivity. None of the studies included to date reported information about vaccination status of recruited participants.

Study design and reference standards

Overall, 72% of studies (n = 109) used a ‘single group’ design to estimate both sensitivity and specificity and 13% (n = 20) used a ‘two group’ design with separate selection of RT-PCR-positive and RT-PCR-negative samples. One study, by Stohr and colleagues, randomized participants between two different RDTs ([Stohr 2021 \[A\]](#); [Stohr 2021 \[B\]](#)). We could not determine study design from the information in five study reports (3%; [Aoki 2021](#); [Dominguez Fernandez 2021](#); [Huh 2021](#); [Liotti 2021](#); [Nash 2020](#)). Sixteen studies included only samples with confirmed SARS-CoV-2, thus only allowing estimation of sensitivity, and one study included only SARS-CoV-2-negative samples allowing estimation of specificity only.

All but two studies defined the presence or absence of SARS-CoV-2 infection based on RT-PCR; one was the ‘specificity only’ study and another used a transcription-mediated amplification (TMA) assay instead of RT-PCR as the reference standard. One hundred and thirty-three (97.8%) studies used a single RT-PCR negative result to confirm absence of infection, including 98 studies in symptomatic or mixed symptom status populations. We did not find any studies requiring two negative RT-PCR results for absence of infection. Two studies used pre-pandemic samples ([Fourati 2020 \[A\]](#); [Veyrenche 2021](#)), and one study used a negative TMA result (n = 1; [Beck 2021](#)).

One hundred and two studies (67%) obtained paired swabs for index and reference standard, 44 (29%) used the same swab for point-of-care and RT-PCR tests and in six studies it was not possible to determine this information from the study report.

Index tests

The 152 studies reported a total of 228 separate test evaluations; 210 of these were comparisons by test brand (and contributed to the overall analysis for this review) and 18 were comparisons using the same test brand with samples from different sites. One hundred and twenty-nine studies evaluated only one test and 23 studies compared two or more tests in the same participants (seven with two tests each, four with three tests, eight with four tests, two with five tests and one each with six or seven tests). The denominator for the index test details in [Table 1](#) is the 210 evaluations by test brand.

The evaluations included 156 (74%) assessments of colloidal gold-based immunoassays (CGIAs); 20 (10%) fluorescent immunoassays (FIAs), 10 using alkaline phosphatase-labelled antibodies; two latex-conjugated LFAs; and four microfluidic FIAs. We could not identify the LFA method for 18 evaluations, either from the study reports or IFUs. Studies evaluated 49 different commercially produced assays (3/49 were nasal kit versions of assays previously intended for naso- or oropharyngeal samples), documented with full assay identification details in Appendix 9. The study reports or manufacturer IFUs for all assays apart from 13 reported

targeting the nucleocapsid protein (Appendix 9). We were unable to identify or obtain IFUs for six assays (those developed by e25bio, Encode/Emmo Pharma, Lepu Medical Technology, Savant Biotech, Sichuan Mass Spectrometry Biotechnology Co., and the SureScreen Diagnostics COVID-19 Antigen Rapid Fluorescent Cassette) and the antigen target was not reported in the IFUs for the remaining seven tests.

Multiple combinations of sample types and use of direct swab testing or swabs in VTM or saline were reported across the evaluations. Based on the evaluations contributing to the overall analysis (n = 210), two-thirds of evaluations (141, 67%) obtained nasopharyngeal samples in all participants, either alone (n = 118, 56%) or in combinations with oropharyngeal samples (23, 11%). A further 12 evaluations (6%) used either nasopharyngeal or oropharyngeal samples in included participants. Nasal samples were used in 44 evaluations: 19 evaluations (9%) used combined nasal and oropharyngeal samples, 13 (6%) used anterior nasal samples, nine (4%) used nasal mid-turbinate samples, and three did not give details about the nasal sample obtained. Other sample sites were used in 10 evaluations (5%), including oropharyngeal alone (n = 3), saliva (n = 3), bronchoalveolar lavage or throat wash (n = 1) and buccal swabs (n = 10).

Fourteen studies provided an additional 18 evaluations of alternative sample sites or test interpretation that are not described in [Table 1](#). Sampling sites included in these evaluations were: anterior nasal (2), nasal mid-turbinate (7), or unspecified nasal samples (2), saliva (5), combined naso-oropharyngeal (1) or oropharyngeal alone (1). The results of these evaluations are included in the comparisons by sample site in [Table 2](#) and Appendix 10.

More than half of studies used direct swab testing (113/210, 54%), 71 (34%) tested samples in VTM or saline, one study used either direct swab testing or VTM and 25 studies (12%), did not provide this information. IFUs for seven assays explicitly recommend against using any transport medium for swab testing (assays from Abbott (Panbio), Anhui Deepblue, Becton Dickinson, Dialab, PCL, Quidel and SD Biosensor; Appendix 9). Twelve assay IFUs provide some form of instructions for use of VTM, and 25 do not mention use of transport medium.

We considered 90 of 210 evaluations (43%) to be compliant with manufacturer IFUs in terms of sample type, use of VTM and time interval between collection and testing. Eighty-one evaluations were judged not compliant with IFUs; 17 used VTM when it was not covered by the IFU, 28 tested samples not listed on the IFUs, and in 57 testing was not always conducted within the one-hour time period specified in the IFU (including 32/57 using samples after a period of frozen storage) (these groupings are not mutually exclusive). We judged IFU compliance to be unclear for 39 evaluations, primarily because we could not determine the time interval between sample collection and testing (n = 27), or because we could not obtain the IFU for the assays evaluated (n = 7); other reasons included use of VTM when the IFU did not specify instructions for using VTM (3), or because the sample site was not reported (n = 1) or use of VTM was not clear (n = 1).

Samples were collected by healthcare workers in 73 (35%) evaluations, were self-collected in 16 (8%), were collected by trained ‘personnel’ or non-healthcare workers in 20 (10%) and by laboratory scientists in nine evaluations. In 89 (42%) the sample

collection was not reported, and in three, individuals with different levels of expertise collected samples.

Samples were tested and interpreted by laboratory scientists in 66 evaluations (31%), by healthcare workers in 50 (24%), by trained 'personnel' or non-healthcare workers in nine (4%) and were self-tested in two evaluations. In 83 of the 210 evaluations the expertise of the test operator was not reported (n = 81, 39%) or was conducted by people with different levels of expertise (n = 2). Of the 83, 47 carried out testing in laboratories, 33 evaluations conducted testing

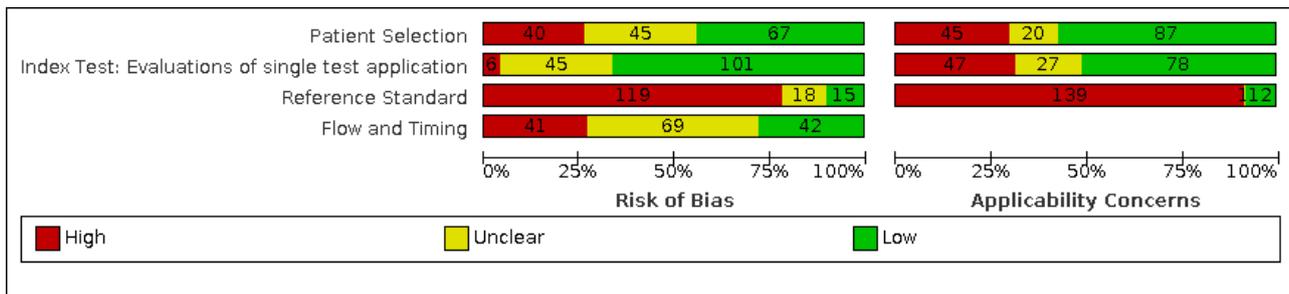
on site and three provided no details of where the tests were conducted.

Methodological quality of included studies

Studies evaluating single test applications

We report the overall methodological quality assessed using the QUADAS-2 tool for all included studies (n = 152) in [Figure 2 \(Whiting 2011\)](#). See Appendix 11 for a plot of study-level ratings by quality domain. We explain how we reached these judgements in the [Characteristics of included studies](#) tables.

Figure 2. Risk of bias and applicability concerns graph for evaluations of single test applications: review authors' judgements about each domain presented as percentages across included studies. Numbers in the bars indicate the number of studies



We considered whether the findings of individual studies were at risk of bias, and whether there were concerns that results might not apply to standard use of the tests. We judged 37 studies to be at low risk of bias for all four domains assessed, four of which also had low concerns about applicability in all domains ([Ferguson 2021](#); [Garcia-Finana 2021](#); [Pilarowski 2021](#); [Schuit 2021\(b\)](#)). These four studies included primarily asymptomatic individuals attending community testing sites, such that a single negative RT-PCR was considered adequate for confirming absence of infection (while two negative results were required for symptomatic participants), and RT-PCR as the sole reference standard was considered sufficient to confirm presence of infection. In 24 of 152 studies the only concern in regard to risk of bias was that a single negative RT-PCR was used to confirm absence of infection rather than the preferred two negative tests for those with signs or symptoms of infection.

Participant selection

We judged 67 studies (44%) to be at low risk of bias for participant sampling. High risk of bias was present in 40 (26%) studies because of deliberate sampling of participants based on the reference standard result (n = 37; including 20 two-group studies and 17 that only included samples with either confirmed SARS-CoV-2 infection or absence of infection) or use of convenience sampling (n = 3). In 45 studies (30%) the risk of bias was unclear because of poor reporting of recruitment procedures or inclusion criteria ([Figure 2](#)).

We judged more than half (87/152, 57%) of studies to have selected an appropriate patient group, recruiting participants from COVID-19 test centres, urgent care or emergency departments or identifying them through contact tracing. We had high concerns about the applicability of the selected participants in 30% of studies (45/152). Recruited participants were unlikely to be similar to those in whom the test would be used in clinical practice because of deliberate sampling based on PCR status (n = 37), use of frozen

samples, or participants recruited from mixed/unclear settings (n = 8).

Index tests

Sixty-six percent of studies had a low risk of bias for the index test (101/152). We judged six studies at high risk of bias because they did not implement blinding of index test interpretation to the reference standard result. Risk of bias was unclear in the remaining 45 (30%) studies because we could not judge whether interpretation of the index test was undertaken with knowledge of the reference standard result.

Just over half of all studies (78/152; 51%) conducted testing as would be expected in practice (low concern regarding applicability). We had high concerns about applicability in 31% of studies (47/152), because at least one test evaluated per study did not comply with manufacturer IFUs. We could not assess the applicability of the index test application for the remaining 27 studies.

Reference standards

Overall, 15 studies were at low risk of bias for the reference standard. High risk of bias was present in 119 studies (78%) because studies did not use an adequate reference standard (single negative RT-PCR used to define absence of SARS-CoV-2 infection in symptomatic populations). Of those studies where we could not judge risk of bias (n = 18), 16 were conducted in predominantly asymptomatic populations and were considered to use an appropriate reference standard, but only one clearly reported blinding of the reference standard to the index test result. Overall, 59 studies reported reference standard blinding.

We had concerns about the applicability of the reference standard in 91% of studies (139/152) because of the reliance on PCR to define

SARS-CoV-2 cases in symptomatic participants. These studies may have considered individuals who were RT-PCR-negative but had exposure and clinical features that met the case definitions for COVID-19 as disease negative. In 12 studies (8%) concerns about applicability were low because they included mainly asymptomatic individuals attending community screening. One study was rated as having unclear concerns for applicability.

Flow and timing

We judged 42 (28%) studies to have low risk of bias for participant flow and timing (Figure 2). Another 41 (27%) were at high risk of bias mainly because of exclusion of samples following invalid index test results (n = 40), including two studies that also reported delays between ‘paired’ swabs of up to three days, or different reference standards used (n = 1). We judged risk of bias to be unclear for 69 (45%) studies, because of lack of clarity about participant inclusion and exclusion from analyses with no missing data or indeterminate test results reported and no Standards for Reporting Diagnostic Accuracy Studies (STARD)-style participant flow diagram and checklist (Bossuyt 2015), to fully report outcomes for all samples.

Conflicts of interest

In 109 studies all authors declared no conflicts of interest, although three of them were directly funded by the company

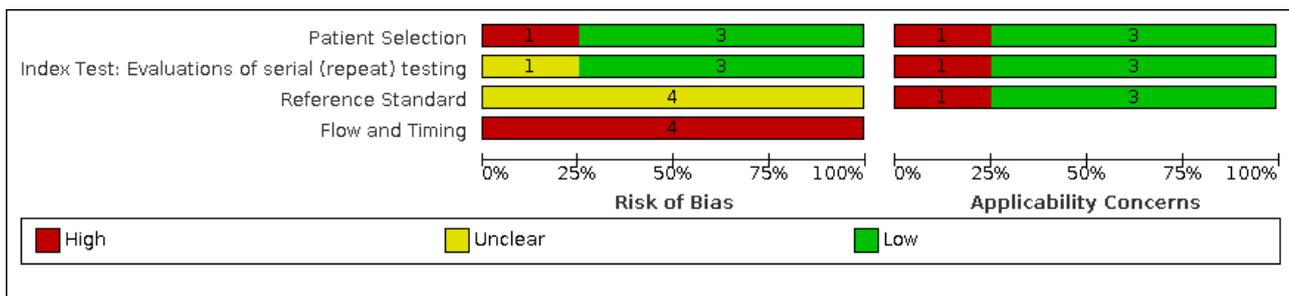
that manufactured the test and nine of them received test kits from the manufacturer. Twenty-four studies did not provide a conflict of interest statement, including 12 published studies. In 19 studies at least one author declared potential conflicts of interest in relation to the evaluation. The remaining studies were independent evaluations such as published by FIND, national reference laboratories, national Public Health Services, Ministry of Health or without any external funding.

Twenty-three studies provided no funding statement, 30 reported no funding sources to declare (of which three studies reported that they received antigen tests from the test manufacturer) and the remainder (n = 99) reported one or more funding sources.

Studies evaluating repeated test applications

We report the overall methodological quality assessed using the QUADAS-2 tool for all included studies that evaluated repeated test applications (n = 4) in Figure 3 (Whiting 2011); one of the four studies is also included in the methodological assessment of studies evaluating a single test application (Kriemler 2021). See Appendix 11 for a plot of study-level ratings by quality domain. We explain how we reached these judgements in the Characteristics of included studies table.

Figure 3. Risk of bias and applicability concerns graph for studies with repeat (serial) testing: review authors' judgements about each domain presented as percentages across included studies



We considered whether the findings of individual studies were at risk of bias, and whether there were concerns that results might not apply to standard use of the tests. None of the four studies were at low risk of bias for all four domains assessed, and one (Winkel 2020), evaluating repeated testing of Dutch footballers, had low concerns about applicability in all domains. In the same study the only concern in regard to risk of bias was that blinding of RT-PCR interpretation to the rapid antigen test result was not clearly reported.

For participant selection, we rated all studies apart from Smith 2021 as having low risk of bias and low concerns for applicability. Smith and colleagues only included participants with PCR positive results and we therefore consider it to have high risk of bias and high concerns for applicability (does not reflect those who might undergo repeat antigen testing in any given population). Smith 2021 also differs from the other three studies in regard to index test risk of bias; all testing was carried out in a laboratory setting within 12 hours of collection and, although likely, it is not fully clear whether index test interpretation was conducted blinded to the result of the reference standard. In contrast only Kriemler 2021 had

high concerns about applicability for the index test because the buccal swab used was not covered on the manufacturer IFU for the assay.

For the reference standard, all studies had unclear risk of bias because they did not report blinding of the reference standard to the index test result. Smith 2021 had high concerns for applicability of the reference standard because all participants were required to have positive viral culture. All studies were considered at high risk of bias because of exclusion of eligible participants from the analysis or because swabs for the index and reference standard were not all obtained within a 12-hour interval of each other.

Findings

We first consider results from studies that evaluated a single application of a rapid antigen test, and then cover results from studies that evaluated repeated antigen testing in the same individuals over time.

Evaluations of single test application

Of the 152 included studies evaluating a single application of a rapid antigen test, 129 evaluated a single brand of antigen test (12/129 comparing sample types and 2/129 evaluating the effect of test operator), and 23 compared the accuracy of two or more different brands of antigen test in the same participants (Table 1). To include all results from all tests in these analyses we have treated results from different tests of the same participants within a study as separate data points, such that data are available on 210 evaluations by test brand and 228 test evaluations when we include comparisons by sample site.

The results tables identify where estimates are based on multiple assessments of the same samples by including both the number of test evaluations and the number of studies. Sixteen studies are 'cases only', reporting only sensitivity estimates and one includes only 'non-COVID-19' cases, reporting only specificity. Summary

results are presented for studies providing both sensitivity and specificity data and then adding in the data from sensitivity- or specificity-only evaluations. The numbers of true positives, false positives, and total samples with and without confirmed SARS-CoV-2 infection are based on test result counts.

We present results of the main analyses and heterogeneity investigations in Table 2, with additional summary results adding in data from 'sensitivity-only' evaluations reported in Appendix 10. Forest plots of study data for the primary analysis (including all evaluations by test brand but excluding comparisons by sample type or test interpretation) are shown in Appendix 12.

Forest plots of data for subgroup analyses in symptomatic and asymptomatic populations are in Figure 4, Figure 5, Figure 6, and by timing of the test in relation to the course of infection in Figure 7 and Figure 8. Data for children are shown in Figure 9, and for subgroups by Ct value or RNA copies/mL in Figure 10 and Figure 11.

Figure 4. Forest plot of data for antigen tests for symptomatic or mainly symptomatic populations. BR: Brazil; CH: Switzerland; DE: Germany; ED: emergency department; HCW: healthcare worker; Lab: laboratory

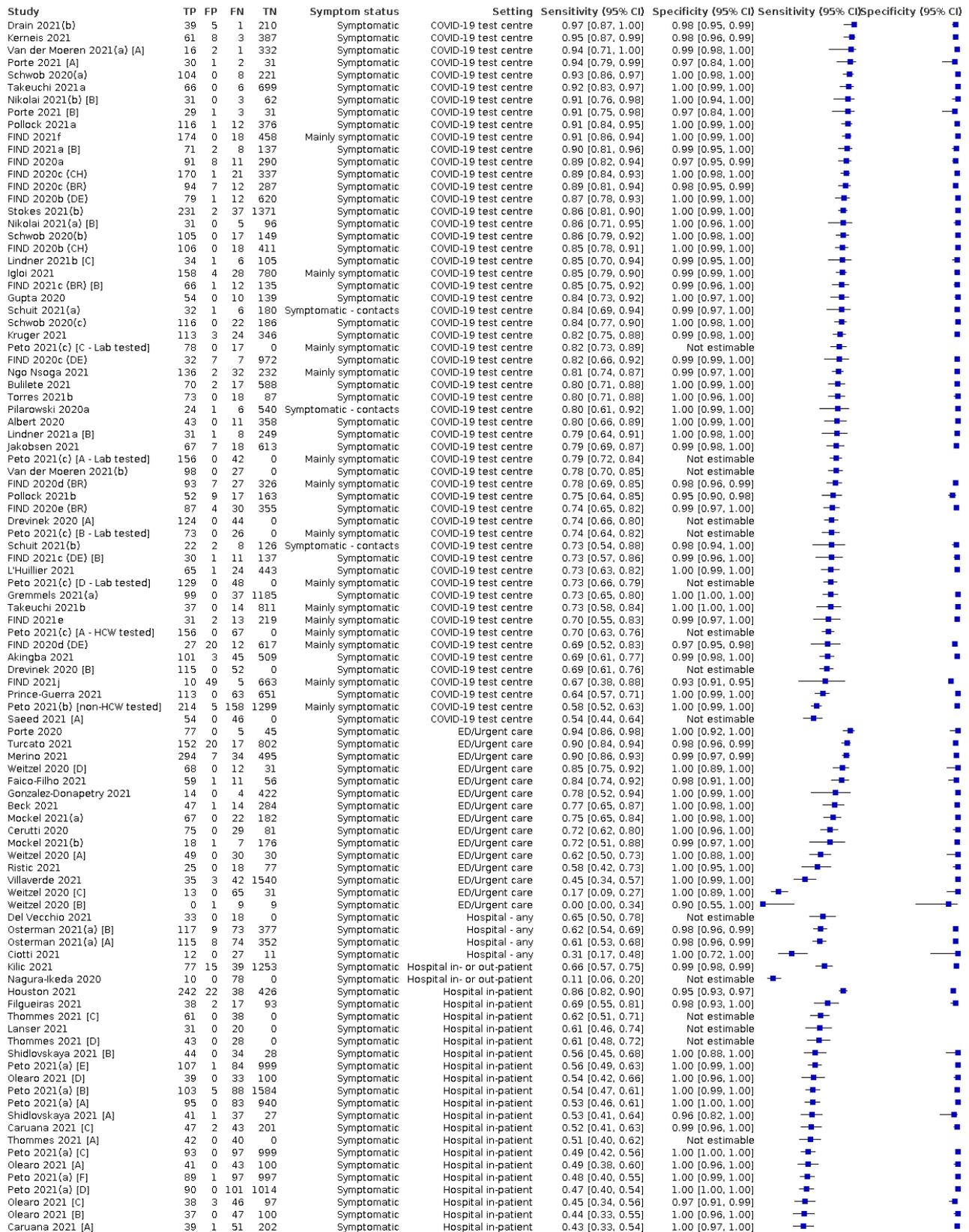


Figure 4. (Continued)

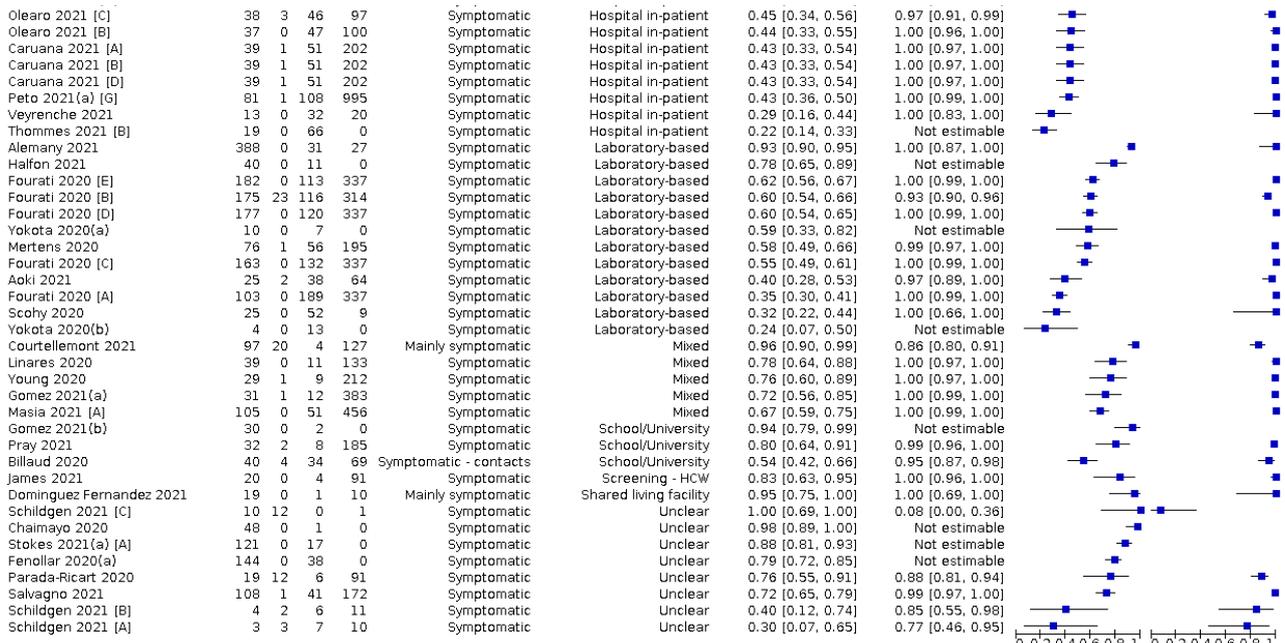


Figure 5. Forest plot of data for antigen tests for asymptomatic or mainly asymptomatic populations: DE: Germany; ED: emergency department; HCW: healthcare worker

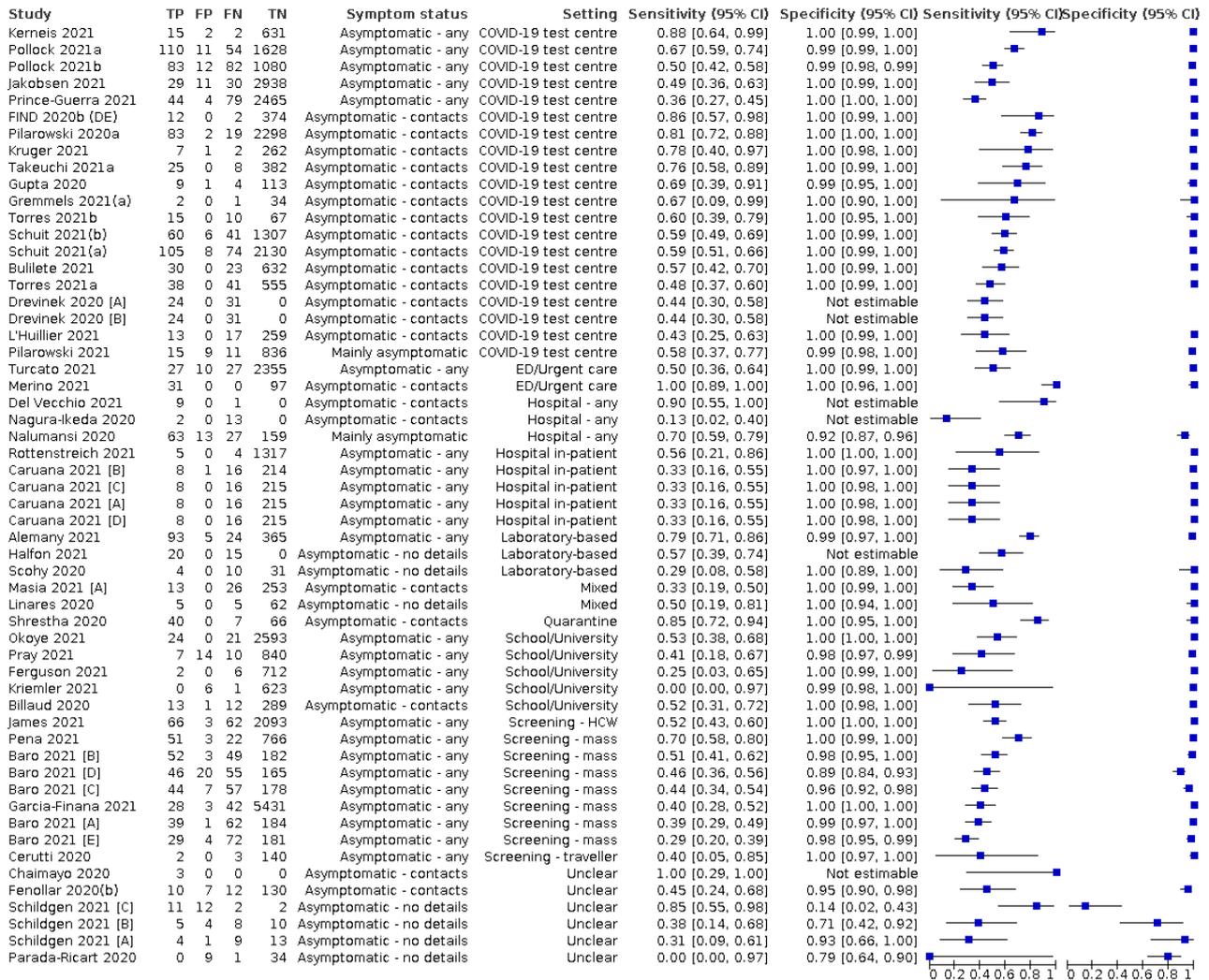
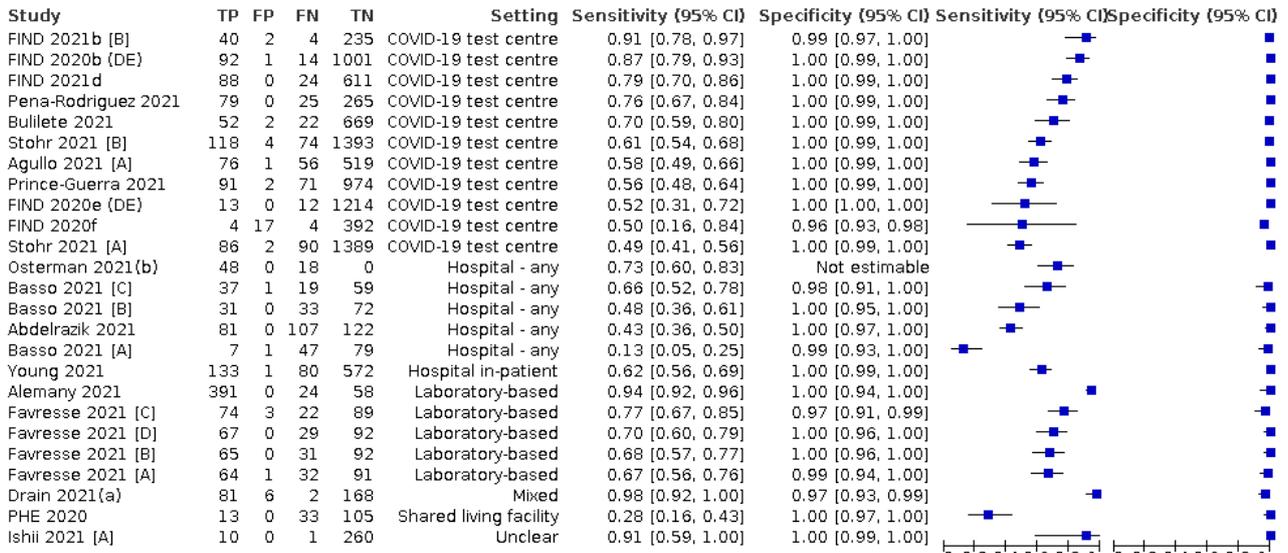


Figure 6. Forest plot of tests: 4 mixed symptom status, 5 symptoms not reported

Mixed symptom status



Symptoms not reported

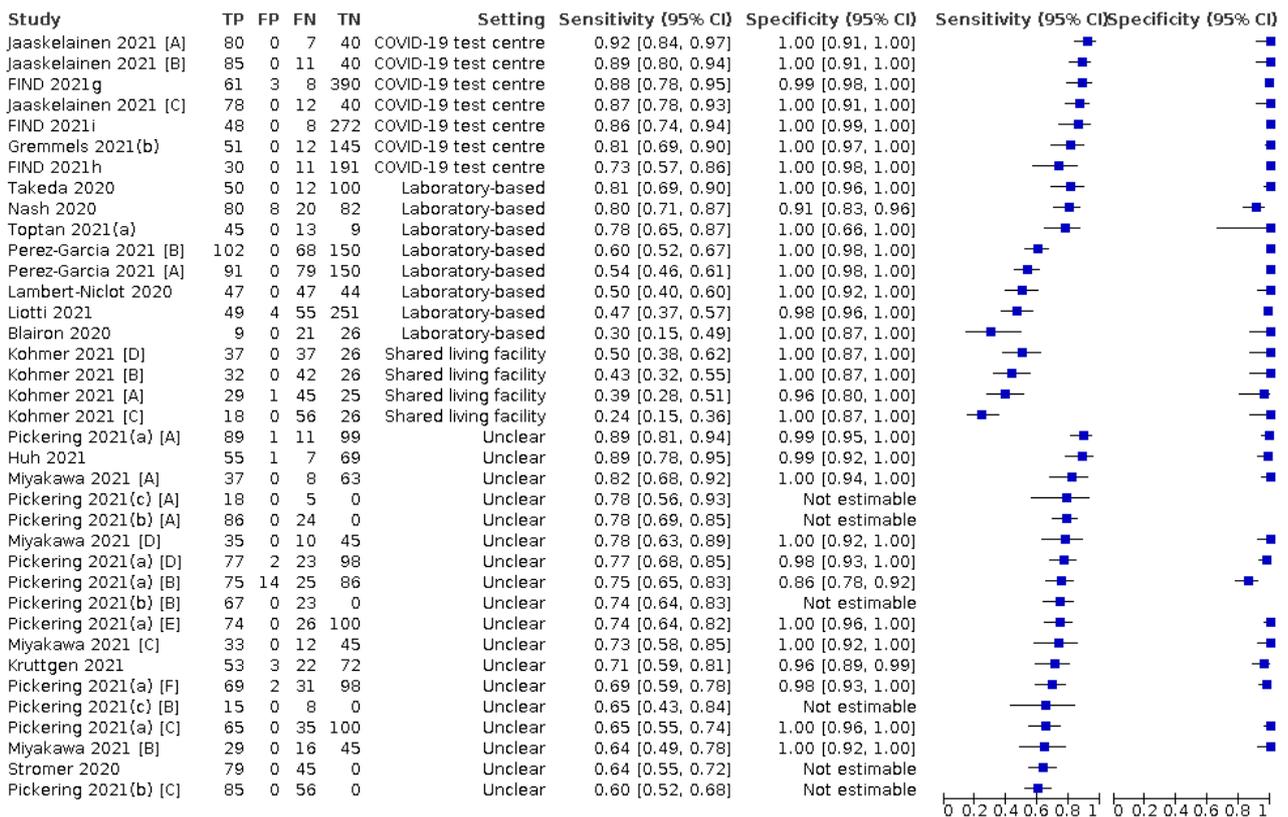
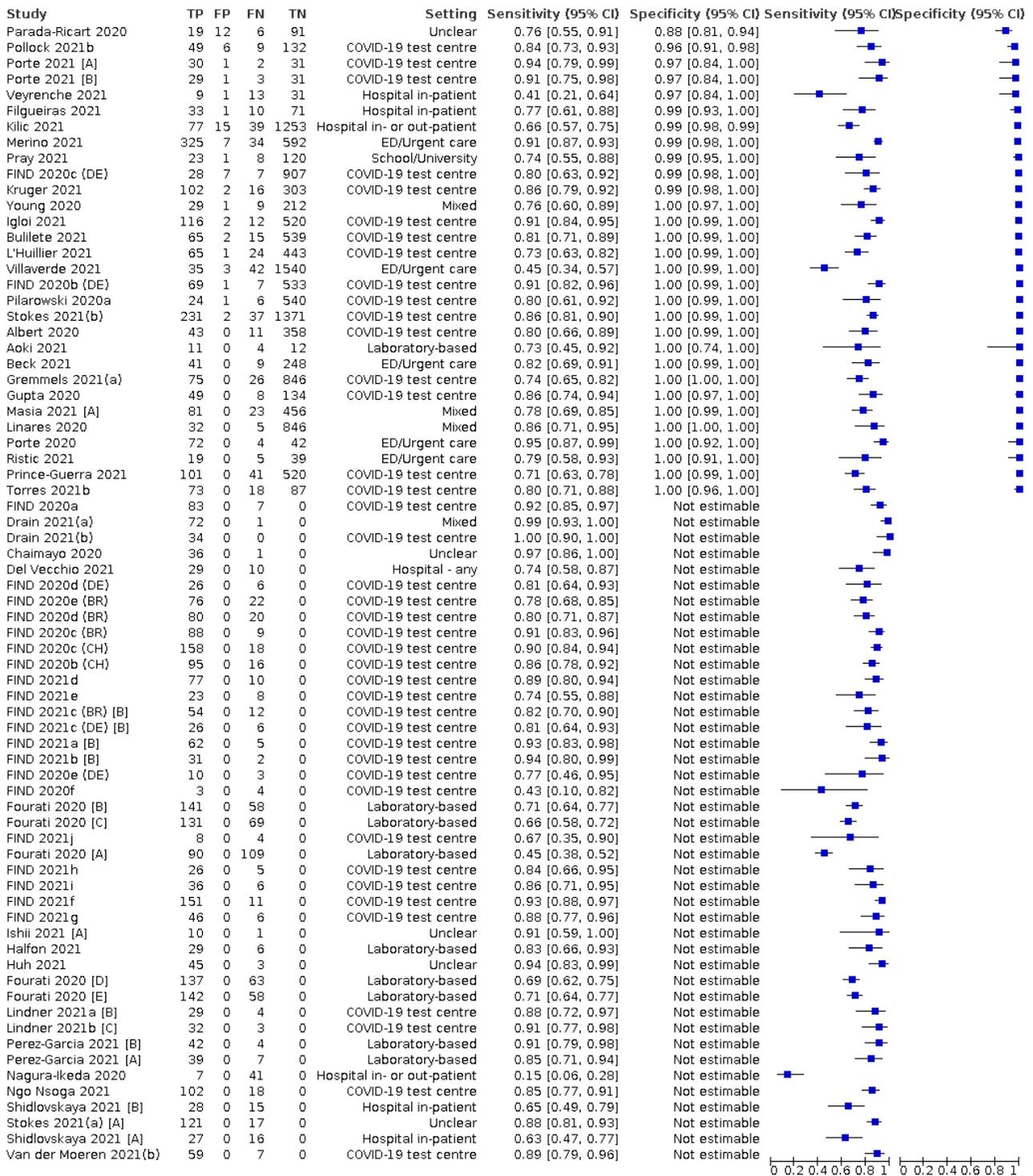


Figure 7. Forest plot of data for symptomatic participants by week post-symptom onset (ps). Ag: antigen; BR: Brazil; CH: Switzerland; DE: Germany; ED: emergency department

Symptomatic - week 1



Symptomatic - week 2

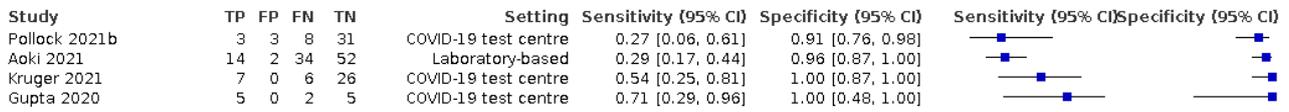


Figure 7. (Continued)

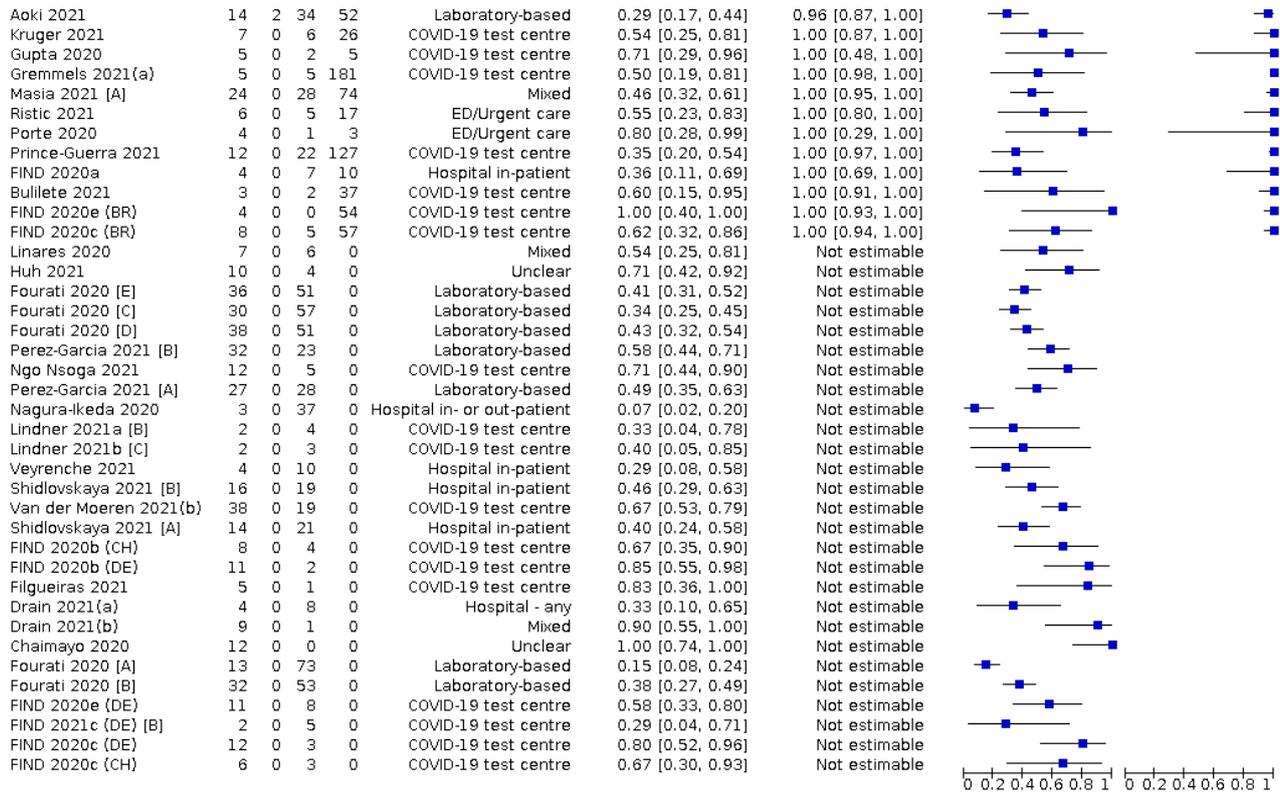


Figure 8. Forest plot of data for asymptomatic participants by week after contact with confirmed case

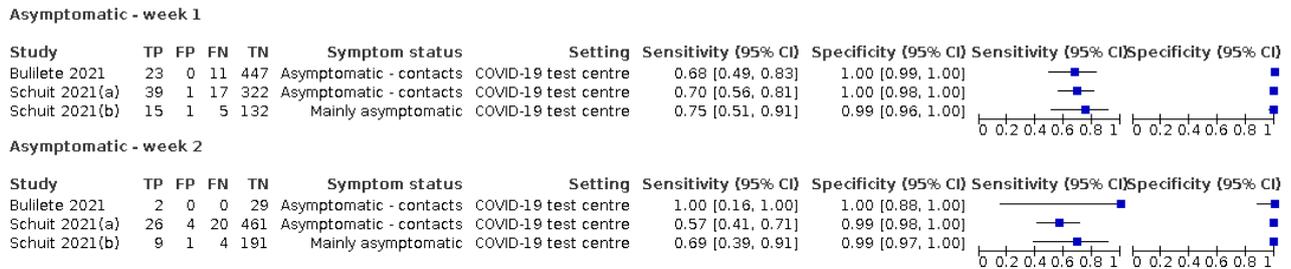


Figure 9. Forest plot of data for accuracy in children and within-study comparison of data for adults (where available)

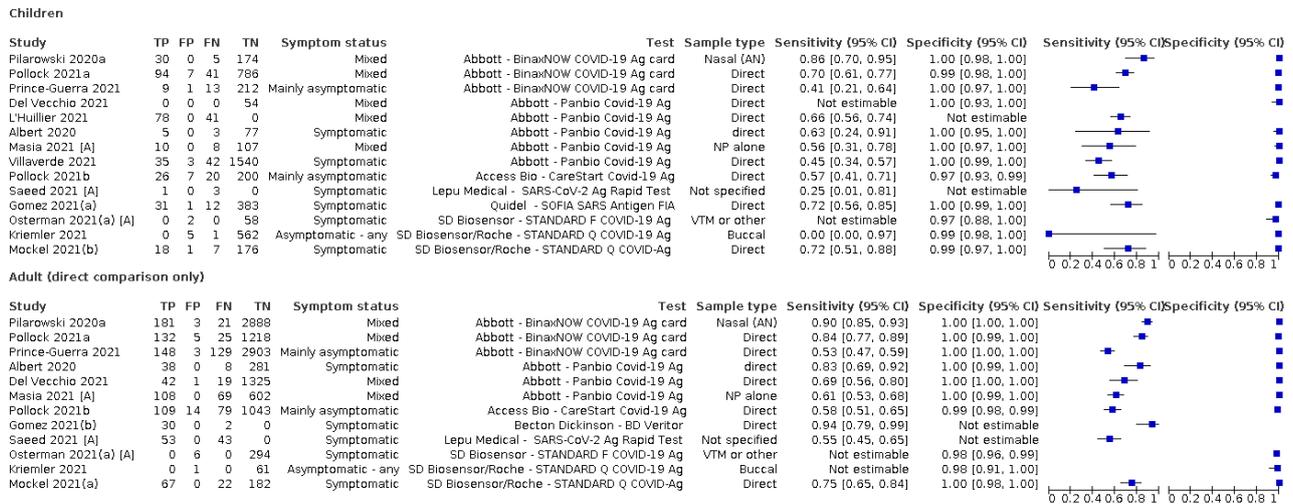
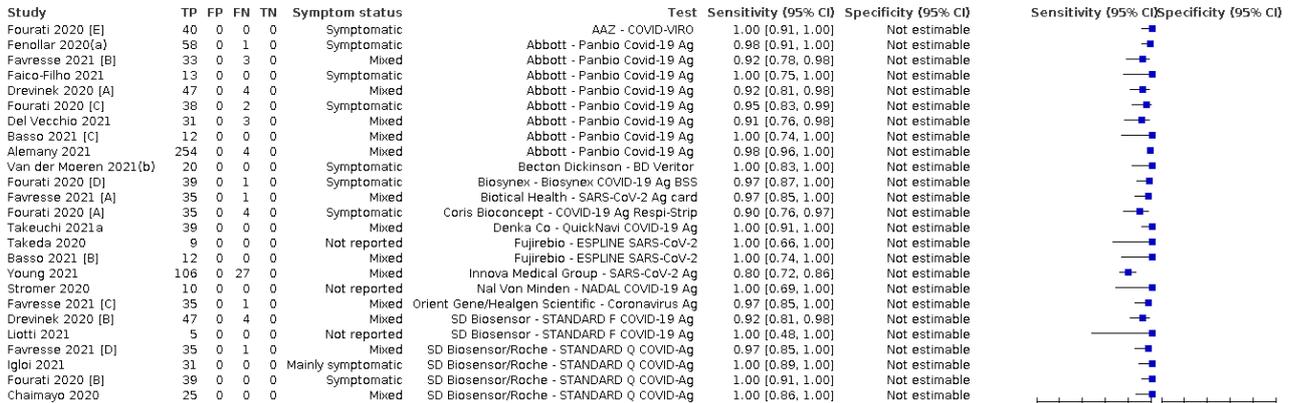
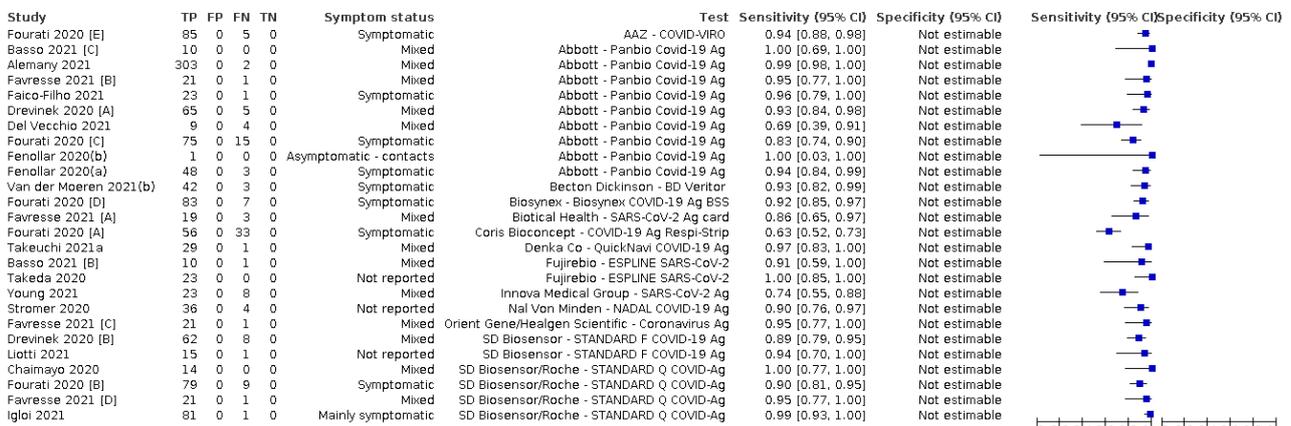


Figure 10. Forest plot of data by viral load (in subgroups by cycle threshold (Ct) value)

Subgroup: < 20 Ct



Subgroup: 20-25 Ct



Subgroup: 25-30 Ct

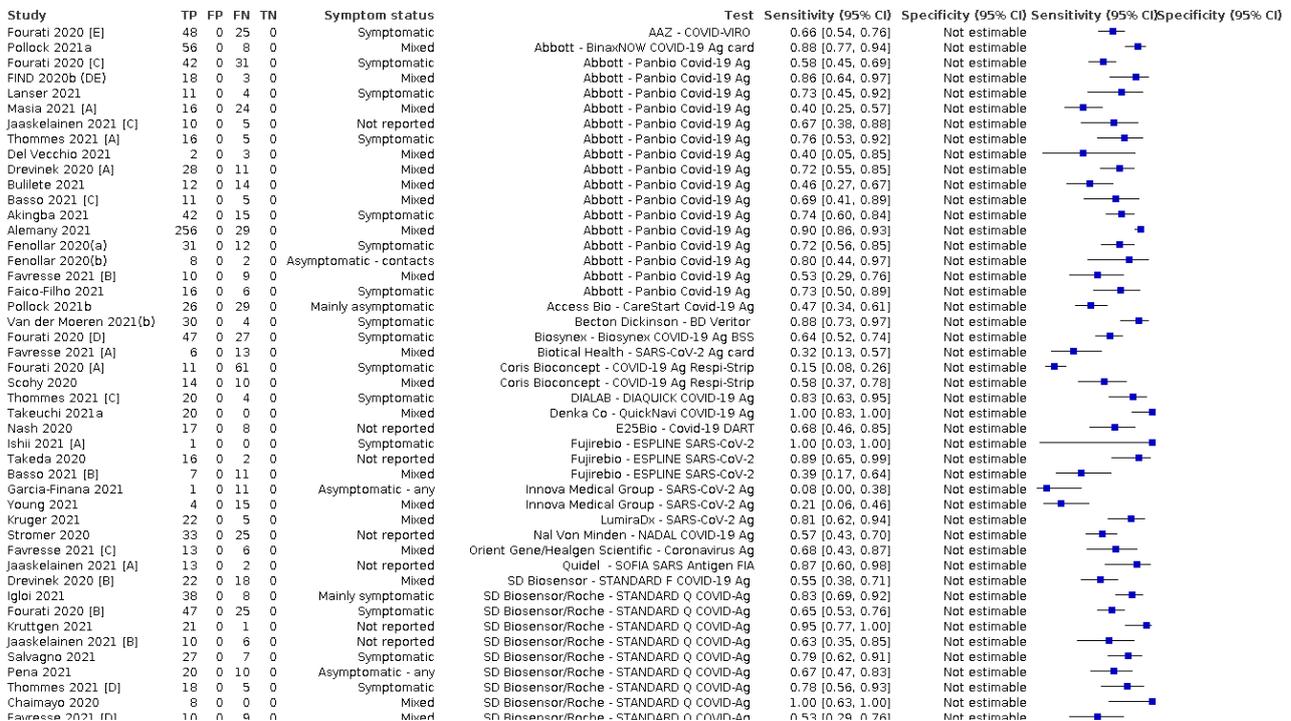


Figure 10. (Continued)

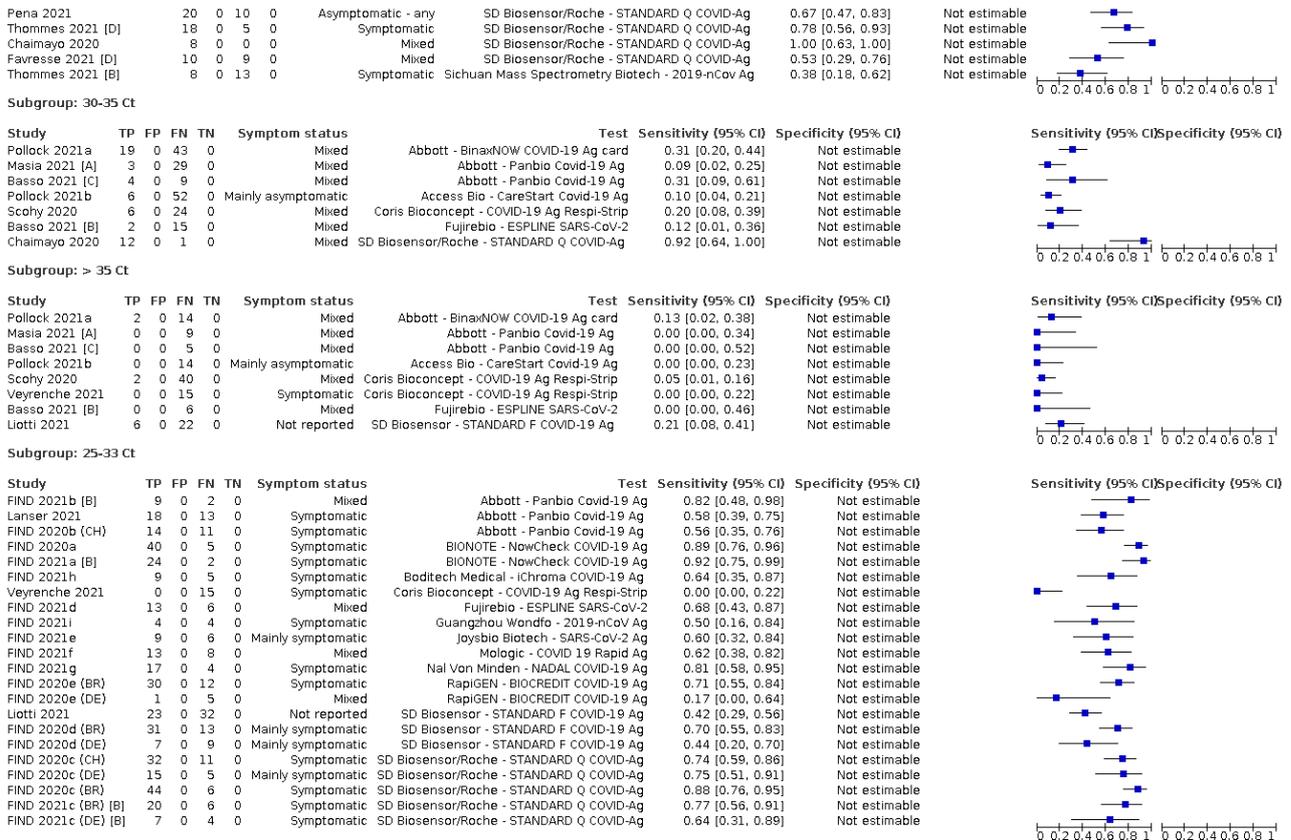


Figure 11. Forest plot of data by viral load (in subgroups by RNA copies/mL)

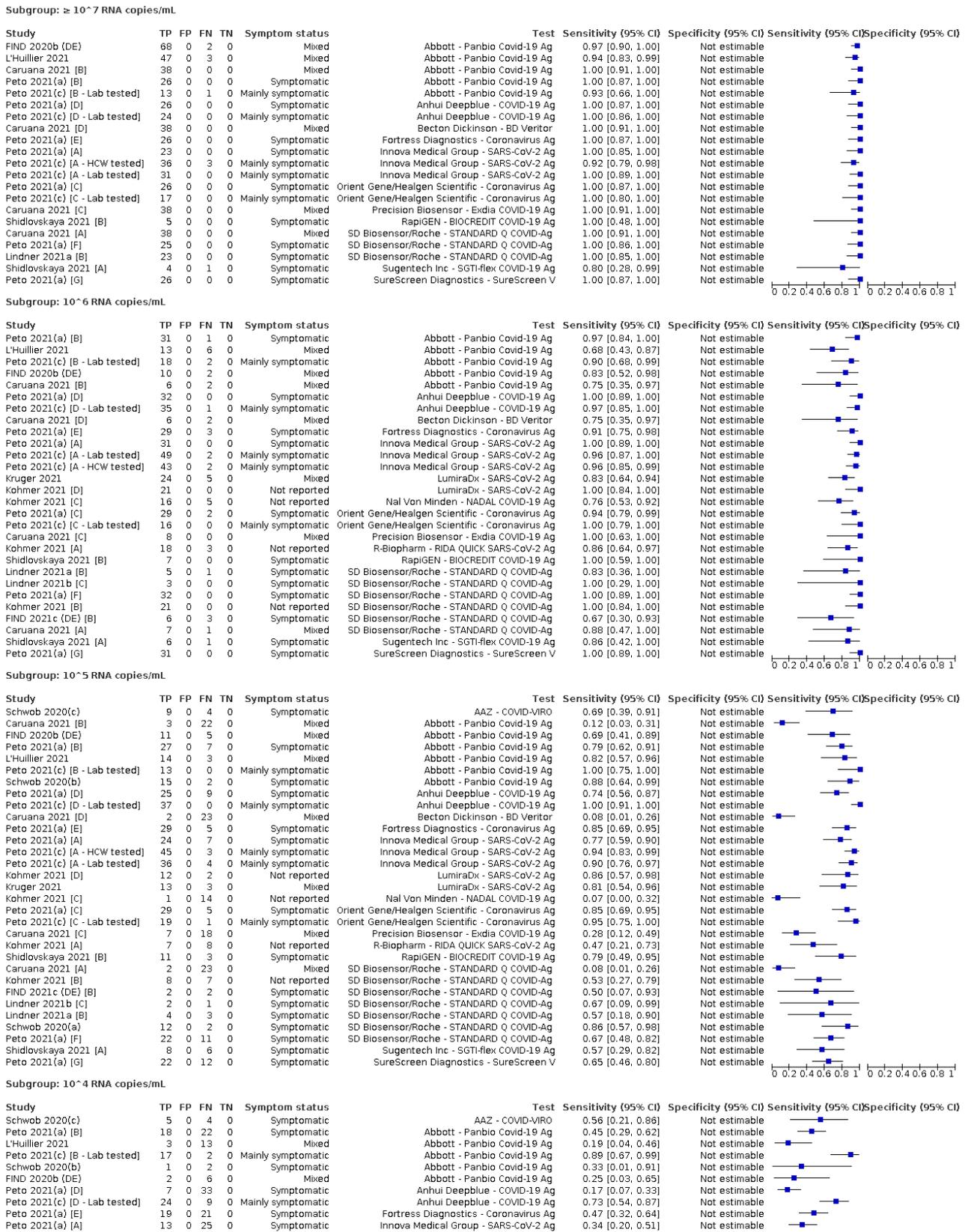


Figure 11. (Continued)

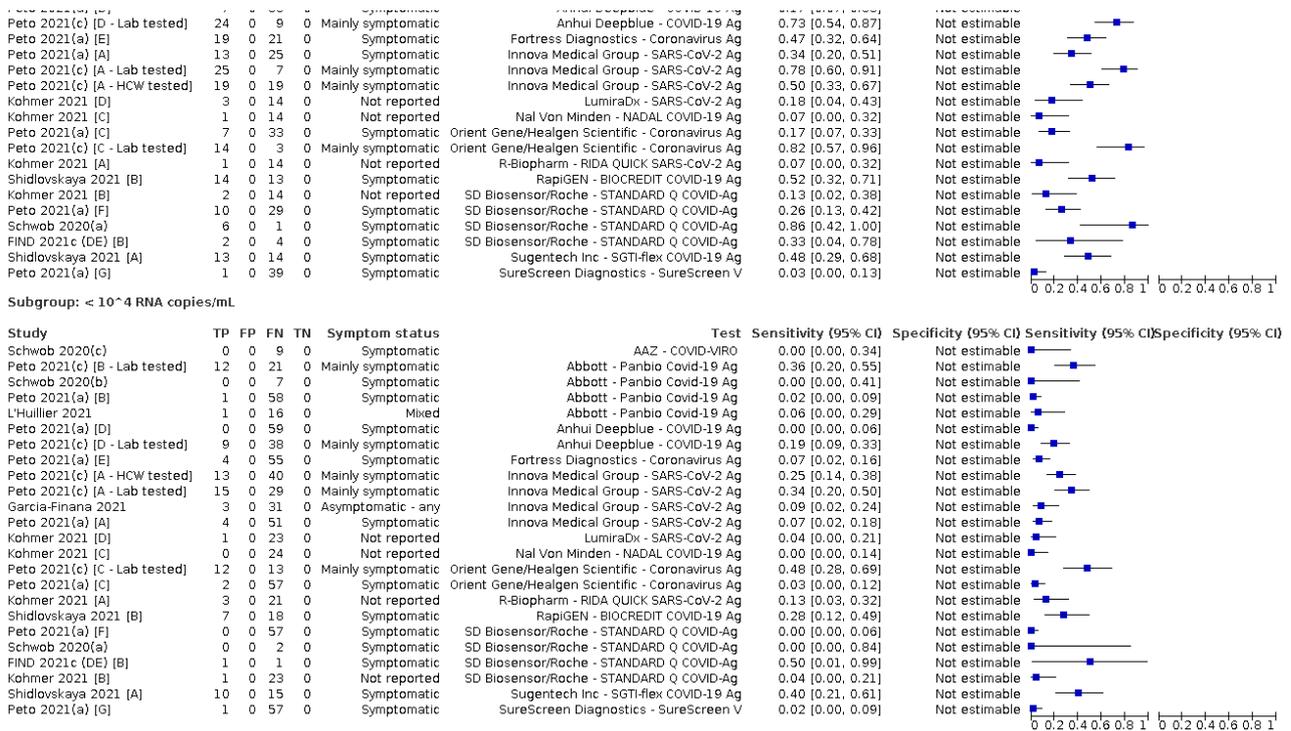


Table 3, Figure 12 and Figure 13 present summary results by test brand according to symptom status, and for sensitivity analyses restricting by compliance with manufacturer IFUs. Forest plots of individual study results by test brand are in Appendix 13 and

summary results by test brand regardless of symptom status are reported in Appendix 14. Within-study comparisons of test brands are reported in Table 4.

Figure 12. Forest plot of results per assay in symptomatic participants (overall and in manufacturer instructions for use (IFU)-compliant evaluations); red lines indicate World Health Organization acceptable and desirable performance standards for sensitivity and specificity in suspected COVID-19 cases

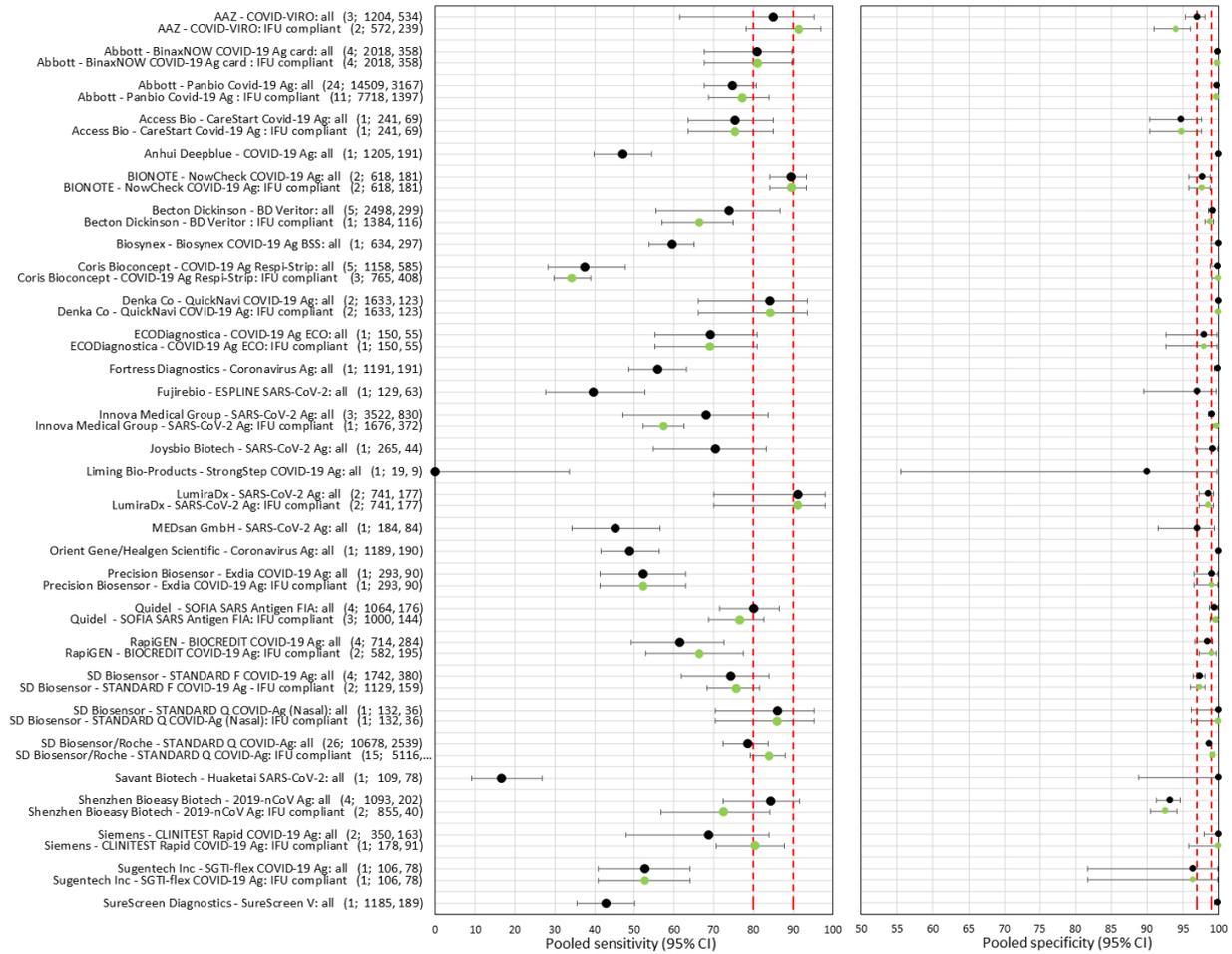
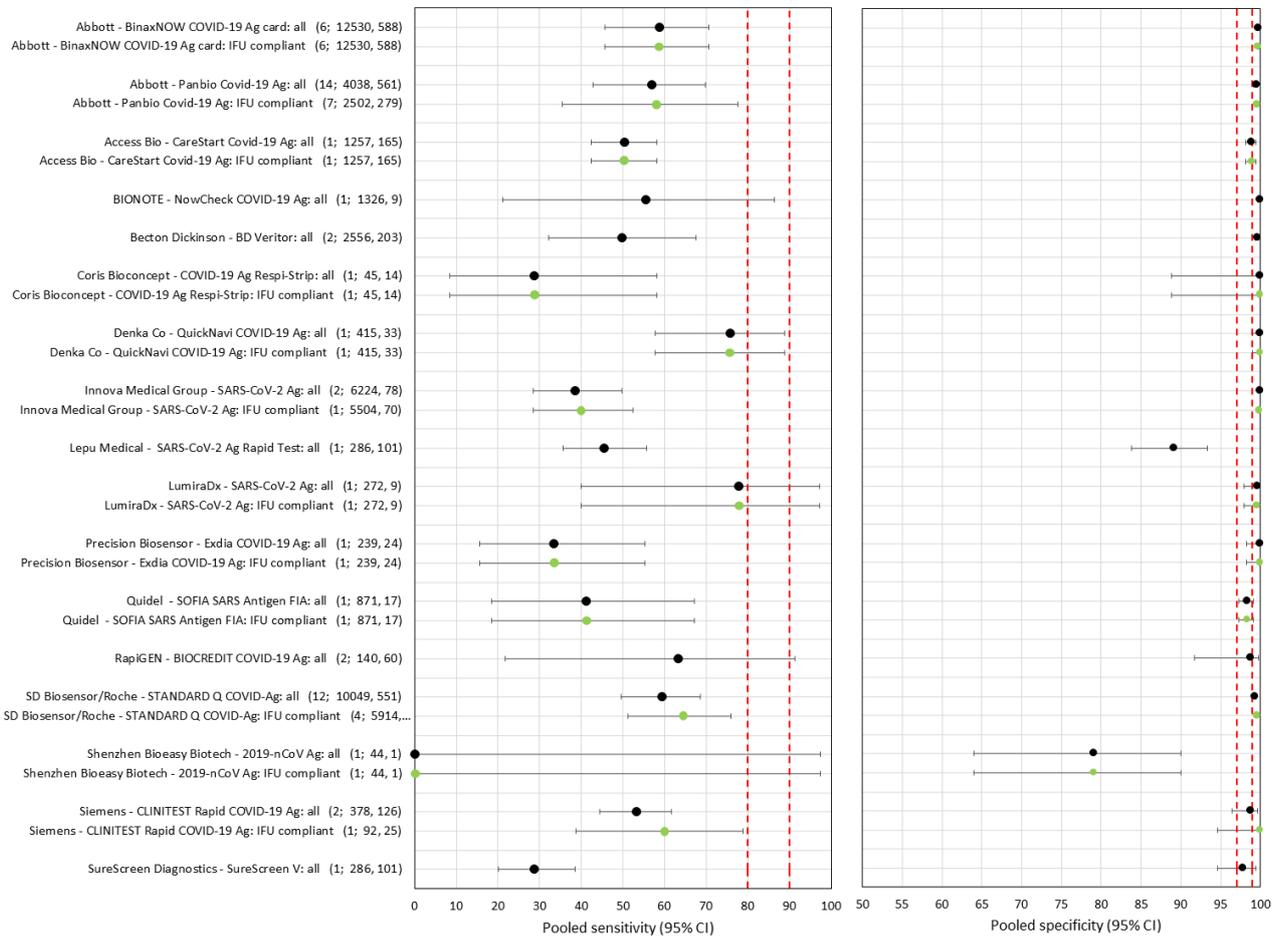


Figure 13. Forest plot of results per assay in asymptomatic participants (overall and in manufacturer instructions for use (IFU)-compliant evaluations); red lines indicate World Health Organization acceptable and desirable performance standards for sensitivity and specificity in suspected COVID-19 cases (there are no performance standards specifically for asymptomatic populations)



Accuracy of antigen tests overall and by subgroup

Results showed high levels of heterogeneity in sensitivity with consistently high specificity (Appendix 12). Average sensitivity was 69.3% (95% CI 66.2% to 72.3%) and average specificity was 99.3% (95% CI 99.2% to 99.3%) across the 184 evaluations of antigen tests reporting both sensitivity and specificity (based on 117,372 samples, including 21,017 samples with confirmed SARS-CoV-2; Table 2). Adding the 25 test evaluations from ‘sensitivity only’ studies and the single ‘specificity only’ dataset had a negligible impact on results (Table 2).

In the sections below we show that there are substantial differences between subgroups of studies according to symptom status, timing, assay format and brand, therefore this average value is unlikely to accurately predict the performance of the test in a given setting and should not be used for this purpose.

Secondary analyses by symptom status

Secondary analysis by symptom status (where possible using subgroup data by symptom status for studies including both symptomatic and asymptomatic participants) suggests that average test sensitivity to detect infection is 18.2 percentage points

lower in asymptomatic participants (54.7%, 95% CI 47.7% to 61.6%; based on 50 evaluations, 40,956 samples and 2,641 cases) compared to symptomatic participants (73.0%, 95% CI 69.3% to 76.4%; based on 109 evaluations, 50,574 samples and 11,662 cases). The 95% CI for the difference in sensitivity ranged from -26.1 to -10.4 percentage points (Table 2; Figure 4 and Figure 5).

Restricting the comparison by symptom status to the 34 evaluations reporting data for both symptomatic and asymptomatic subgroups (thus ensuring the comparison is made between the same tests used in the same way) showed a similar difference in sensitivity (Table 2). Inclusion of data from sensitivity-only cohorts led to a small increase in the difference in sensitivity (Table 2).

Specificity was marginally higher in asymptomatic populations, both overall (0.4 percentage points higher) and for within-study comparisons (0.5 percentage points higher; Table 2).

Average results for the 56 evaluations in participants with mixed symptom status (n = 25) or symptom status not reported (n = 31) were similar to those observed for the symptomatic participants (Table 2; Figure 6), suggesting these studies may have included

mainly symptomatic individuals: sensitivity 70.6% (95% CI 64.8% to 75.3%) and specificity 99.4% (95% CI 99.3% to 99.5%) based on 9359 samples and 5344 cases.

Adding the test evaluations from 'sensitivity-only' studies (23 in symptomatic participants, 6 in asymptomatic participants and 7 in mixed symptom populations) had a negligible impact on results (Appendix 10).

Subgroup analysis for symptomatic participants by study by setting

Statistical evidence for a difference in sensitivity was observed for symptomatic participants according to study setting (Table 2; Figure 4). Average sensitivity in COVID-19 test centres was 82.8% (95% CI 80.2% to 85.2%) and specificity 99.1% (95% CI 99.0% to 99.2%); 47 evaluations in 23,602 samples, including 4369 cases). Average sensitivity was lower in all other settings considered; the absolute difference ranged from 11.9 percentage points lower for those presenting in emergency departments or urgent care centres (95% CI 25.7 percentage points lower to 1.9 higher) to 31.3 percentage points lower for hospital inpatients (95% CI from -37.5 to -25.1 percentage points). Results varied in other settings (hospitals in- or outpatients, healthcare worker screening, and shared living facility settings), but with only one evaluation each (Table 2).

Adding data from the 14 test evaluations from 'sensitivity-only' studies had a small effect on average sensitivity for all settings (changes of up to 3 percentage points) apart from testing of symptomatic participants in school or university settings. Average sensitivity increased considerably when the number of included evaluations for schools or university settings increased from two to three however the number of cases ($n = 146$) remained low (Appendix 10).

Subgroup analysis for symptomatic participants by time from symptom onset

A total of 72 test evaluations reported data for symptomatic participants according to time after the onset of symptoms (week 1 compared to week 2 or later; Table 2; Figure 7). In contrast to the previous iteration of this review, considerably more ($n = 30$) studies provided results for both sensitivity and specificity according to time from onset of symptoms (compared to 10 for the previous version), and the remaining 42 provided data only for confirmed SARS-CoV-2 cases (so that only sensitivity could be calculated).

Where both sensitivity and specificity could be calculated, in week one after symptom onset average sensitivity was 80.9% (95% CI 76.9% to 84.4%), and specificity 99.5% (95% CI 99.3% to 99.6%); based on 30 evaluations including 15,323 samples and 2408 cases). In week two or later after onset, average sensitivity was 48.9% (95% CI 37.9% to 60.1%) and specificity 99.3% (95% CI 98.2% to 99.7%) based on 13 evaluations including 903 samples and 224 cases (Table 2). Average sensitivity was 32.0 percentage points lower at the later time point (95% CI -43.9 to -20.1 percentage points).

Including the 42 evaluations that provided data only for sensitivity by time after onset led to small increases in average sensitivity during both time periods (Table 2). The difference in sensitivity between time points decreased slightly to -28.4 percentage points (95% CI from -32.6 to -24.2 percentage points lower in week two compared to week one after onset), based on 5640 cases in week one and 1119 cases in week 2.

Subgroup analyses for asymptomatic participants by eligibility for testing and study setting

Subgroup analyses for asymptomatic participants indicated that sensitivity was higher when an epidemiological exposure to SARS-CoV-2 was suspected (based on studies reporting specific criteria for testing or referral for testing of those without symptoms) compared to where COVID-19 testing was reported to be widely available to any asymptomatic participant on presentation for testing (Table 2; Figure 5). The absolute difference in sensitivity was 14.7 percentage points (95% CI from 2.7 to 26.7 percentage points) when an epidemiological exposure to SARS-CoV-2 was suspected (sensitivity 64.3%, 95% CI 54.6% to 73.0% compared to 49.6%, 95% CI 42.1% to 57.1%; based on 16 evaluations in 7677 samples with 703 cases and 26 evaluations with 31,904 samples and 1758 cases respectively). Average specificity was similarly high (99.6% or 99.7%) regardless of the presence or absence of likely epidemiological exposure (0.06 percentage points difference, 95% CI from -0.09 to 0.22; Table 2).

Adding data from sensitivity-only cohorts led to a slight decrease in the difference in sensitivity between widely available testing and testing of contacts; difference 12.2 percentage points (95% CI 0.2 to 24.2 percentage points higher in the contacts group (Table 2).

Analyses for asymptomatic participants by study setting were limited by the number of studies per group and low numbers of confirmed SARS-CoV-2 cases for some subgroups, however average sensitivities were highest for participants presenting to COVID-19 test centres (61.5%, 95% CI 54.0% to 68.4%; based on 18 evaluations including 19,253 samples and 1195 cases) or emergency care settings (average sensitivity 95.1%, 95% CI 7.3% to 100%; based on 2 evaluations with 2547 samples and 85 cases; Table 2; Figure 5). For the seven evaluations considered to represent screening scenarios, average sensitivity was 45.1% (95% CI 36.4% to 54.1%; based on 7776 samples and 648 cases of SARS-CoV-2); for school or university-wide testing programmes it was 47.9% (95% CI 38.1% to 57.9%; 5 evaluations, including 5174 samples and 96 cases); and for blanket testing of hospital inpatients with no apparent symptoms of COVID-19 it was 35.2% (95% CI 26.7% to 44.8%; based on 5 evaluations including 2282 samples and 105 cases). Adding the test evaluations from 'sensitivity-only' studies had a negligible impact on results (Appendix 10).

Three evaluations in asymptomatic or mainly asymptomatic contacts of confirmed cases reported sensitivity and specificity by reported time after contact (1013 samples and 110 cases in week 1 and 747 samples and 61 cases in week 2; Table 2; Figure 8). Sensitivity was 70.0% in week 1 (95% CI 60.8% to 77.8%) compared to 60.7% in week 2 (95% CI 48.0% to 72.0%), however the 95% CI for the difference between time points was from 24.3 percentage points lower to 5.6 higher, suggesting no statistical evidence for a difference.

Sensitivity analysis by study design

Restricting study inclusion to those using single group designs had only a marginal effect on summary sensitivity (70.8%, 95% CI 67.2% to 74.3%) and specificity (99.4%, 95% CI 99.3% to 99.4%), based on 93,970 samples and 14,171 cases from 126 evaluations; Table 2; Appendix 12 see Figure 14).

Figure 14. Forest plot of data by study design. BR: Brazil; CH: Switzerland; DE: Germany; HCW: healthcare worker

Antigen test evaluations - Single group design (sensitivity and specificity)

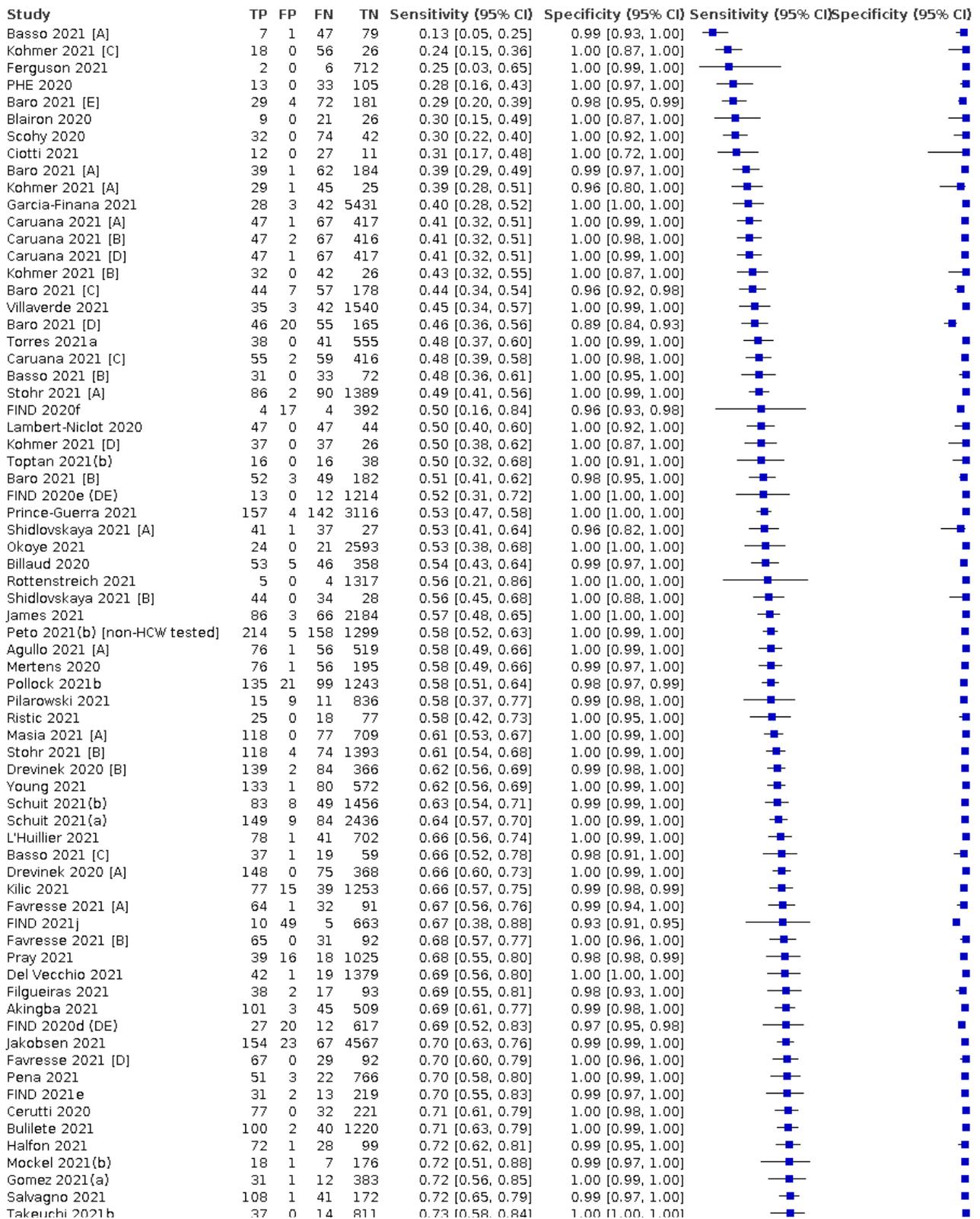
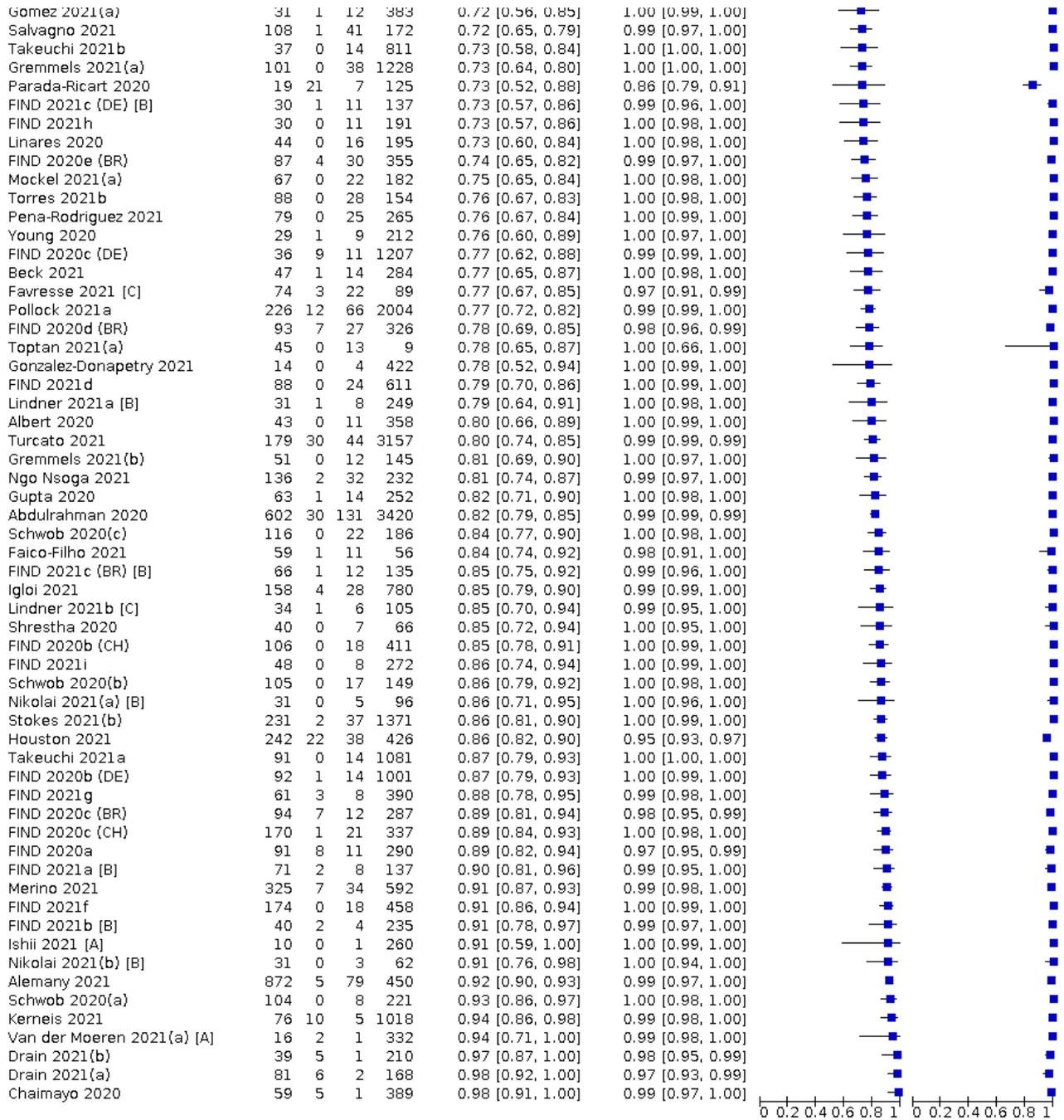


Figure 14. (Continued)

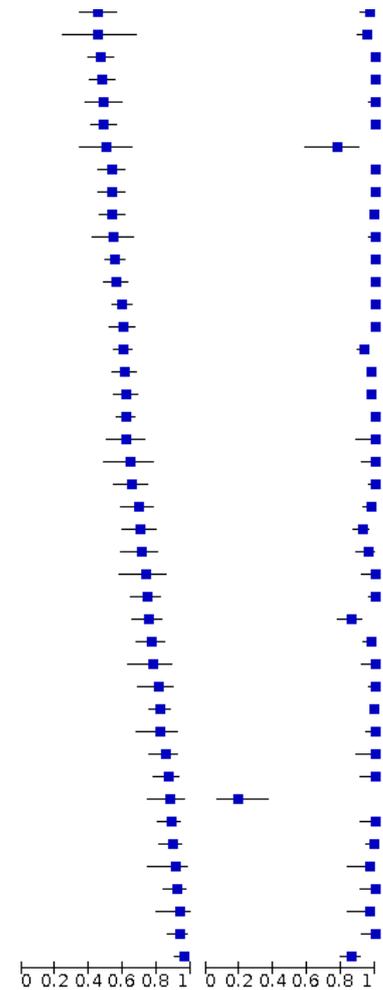


Antigen test evaluations - Two group design

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Weitzel 2020 [B]	0	1	9	9	0.00 [0.00, 0.34]	0.90 [0.55, 1.00]		
Weitzel 2020 [C]	13	0	65	31	0.17 [0.09, 0.27]	1.00 [0.89, 1.00]		
Veyrenche 2021	13	0	32	20	0.29 [0.16, 0.44]	1.00 [0.83, 1.00]		
Schildgen 2021 [A]	14	4	28	27	0.33 [0.20, 0.50]	0.87 [0.70, 0.96]		
Fourati 2020 [A]	103	0	189	337	0.35 [0.30, 0.41]	1.00 [0.99, 1.00]		
Peto 2021(a) [G]	81	1	108	995	0.43 [0.36, 0.50]	1.00 [0.99, 1.00]		
Abdelrazik 2021	81	0	107	122	0.43 [0.36, 0.50]	1.00 [0.97, 1.00]		
Oleairo 2021 [B]	37	0	47	100	0.44 [0.33, 0.55]	1.00 [0.96, 1.00]		
Oleairo 2021 [C]	38	3	46	97	0.45 [0.34, 0.56]	0.97 [0.91, 0.99]		
Fenollar 2020(b)	10	7	12	130	0.45 [0.24, 0.68]	0.95 [0.90, 0.98]		
Peto 2021(a) [D]	90	0	101	1014	0.47 [0.40, 0.54]	1.00 [1.00, 1.00]		

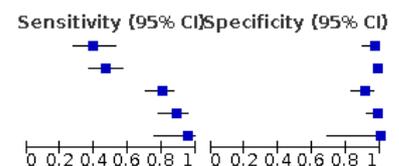
Figure 14. (Continued)

Olearo 2021 [C]	38	3	46	97	0.45 [0.34, 0.56]	0.97 [0.91, 0.99]
Fenollar 2020(b)	10	7	12	130	0.45 [0.24, 0.68]	0.95 [0.90, 0.98]
Peto 2021(a) [D]	90	0	101	1014	0.47 [0.40, 0.54]	1.00 [1.00, 1.00]
Peto 2021(a) [F]	89	1	97	997	0.48 [0.40, 0.55]	1.00 [0.99, 1.00]
Olearo 2021 [A]	41	0	43	100	0.49 [0.38, 0.60]	1.00 [0.96, 1.00]
Peto 2021(a) [C]	93	0	97	999	0.49 [0.42, 0.56]	1.00 [1.00, 1.00]
Schildgen 2021 [B]	21	7	21	24	0.50 [0.34, 0.66]	0.77 [0.59, 0.90]
Peto 2021(a) [A]	95	0	83	940	0.53 [0.46, 0.61]	1.00 [1.00, 1.00]
Perez-Garcia 2021 [A]	91	0	79	150	0.54 [0.46, 0.61]	1.00 [0.98, 1.00]
Peto 2021(a) [B]	103	5	88	1584	0.54 [0.47, 0.61]	1.00 [0.99, 1.00]
Olearo 2021 [D]	39	0	33	100	0.54 [0.42, 0.66]	1.00 [0.96, 1.00]
Fourati 2020 [C]	163	0	132	337	0.55 [0.49, 0.61]	1.00 [0.99, 1.00]
Peto 2021(a) [E]	107	1	84	999	0.56 [0.49, 0.63]	1.00 [0.99, 1.00]
Fourati 2020 [D]	177	0	120	337	0.60 [0.54, 0.65]	1.00 [0.99, 1.00]
Perez-Garcia 2021 [B]	102	0	68	150	0.60 [0.52, 0.67]	1.00 [0.98, 1.00]
Fourati 2020 [B]	175	23	116	314	0.60 [0.54, 0.66]	0.93 [0.90, 0.96]
Osterman 2021(a) [A]	115	8	74	352	0.61 [0.53, 0.68]	0.98 [0.96, 0.99]
Osterman 2021(a) [B]	117	9	73	377	0.62 [0.54, 0.69]	0.98 [0.96, 0.99]
Fourati 2020 [E]	182	0	113	337	0.62 [0.56, 0.67]	1.00 [0.99, 1.00]
Weitzel 2020 [A]	49	0	30	30	0.62 [0.50, 0.73]	1.00 [0.88, 1.00]
Miyakawa 2021 [B]	29	0	16	45	0.64 [0.49, 0.78]	1.00 [0.92, 1.00]
Pickering 2021(a) [C]	65	0	35	100	0.65 [0.55, 0.74]	1.00 [0.96, 1.00]
Pickering 2021(a) [F]	69	2	31	98	0.69 [0.59, 0.78]	0.98 [0.93, 1.00]
Nalumansi 2020	63	13	27	159	0.70 [0.59, 0.79]	0.92 [0.87, 0.96]
Kruttgen 2021	53	3	22	72	0.71 [0.59, 0.81]	0.96 [0.89, 0.99]
Miyakawa 2021 [C]	33	0	12	45	0.73 [0.58, 0.85]	1.00 [0.92, 1.00]
Pickering 2021(a) [E]	74	0	26	100	0.74 [0.64, 0.82]	1.00 [0.96, 1.00]
Pickering 2021(a) [B]	75	14	25	86	0.75 [0.65, 0.83]	0.86 [0.78, 0.92]
Pickering 2021(a) [D]	77	2	23	98	0.77 [0.68, 0.85]	0.98 [0.93, 1.00]
Miyakawa 2021 [D]	35	0	10	45	0.78 [0.63, 0.89]	1.00 [0.92, 1.00]
Takeda 2020	50	0	12	100	0.81 [0.69, 0.90]	1.00 [0.96, 1.00]
Kruger 2021	120	4	26	611	0.82 [0.75, 0.88]	0.99 [0.98, 1.00]
Miyakawa 2021 [A]	37	0	8	63	0.82 [0.68, 0.92]	1.00 [0.94, 1.00]
Weitzel 2020 [D]	68	0	12	31	0.85 [0.75, 0.92]	1.00 [0.89, 1.00]
Jaaskelainen 2021 [C]	78	0	12	40	0.87 [0.78, 0.93]	1.00 [0.91, 1.00]
Schildgen 2021 [C]	37	25	5	6	0.88 [0.74, 0.96]	0.19 [0.07, 0.37]
Jaaskelainen 2021 [B]	85	0	11	40	0.89 [0.80, 0.94]	1.00 [0.91, 1.00]
Pickering 2021(a) [A]	89	1	11	99	0.89 [0.81, 0.94]	0.99 [0.95, 1.00]
Porte 2021 [B]	29	1	3	31	0.91 [0.75, 0.98]	0.97 [0.84, 1.00]
Jaaskelainen 2021 [A]	80	0	7	40	0.92 [0.84, 0.97]	1.00 [0.91, 1.00]
Porte 2021 [A]	30	1	2	31	0.94 [0.79, 0.99]	0.97 [0.84, 1.00]
Porte 2020	77	0	5	45	0.94 [0.86, 0.98]	1.00 [0.92, 1.00]
Courtellemont 2021	97	20	4	127	0.96 [0.90, 0.99]	0.86 [0.80, 0.91]



Antigen test evaluations - Unclear design

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aoki 2021	25	2	38	64	0.40 [0.28, 0.53]	0.97 [0.89, 1.00]
Liotti 2021	49	4	55	251	0.47 [0.37, 0.57]	0.98 [0.96, 1.00]
Nash 2020	80	8	20	82	0.80 [0.71, 0.87]	0.91 [0.83, 0.96]
Huh 2021	55	1	7	69	0.89 [0.78, 0.95]	0.99 [0.92, 1.00]
Dominguez Fernandez 2021	19	0	1	10	0.95 [0.75, 1.00]	1.00 [0.69, 1.00]



Subgroup analysis by sample site

We observed some difference in accuracy according to the type of sample used, however observed differences may be confounded by a number of factors including the populations studied, timing of tests in regard to course of infection and variations in accuracy of the tests used. Results are therefore presented based on subgroup analysis of all data contributing to the primary analysis and then restricted to the small number of evaluations comparing accuracy by sample site in some or all participants, that is, studies used the same rapid antigen test on samples from two different sites (Table 2). Differences in the number of samples per site were observed for some studies such that we are not able to present data for strictly 'paired' comparisons.

The majority of evaluations (n = 128 for studies reporting both sensitivity and specificity) obtained nasopharyngeal samples from all study participants, either as the sole sample site, or in combination with oropharyngeal sampling in some or all participants. Average sensitivity was 69.0% (95% CI 65.3% to 72.4%) and average specificity 99.4% (95% CI 99.3% to 99.4%) in 59,447 samples including 13,270 cases of SARS-CoV-2; Table 2; Appendix 12 see Figure 15). Average sensitivity in studies using nasal samples (anterior nasal in 14, nasal mid-turbinate in 15, and not further specified in 5) was 76.6% (95% CI 70.3% to 81.9%; in 33,128 samples including 4032 cases); an increase of 7.7 percentage points compared to studies in the nasopharyngeal sample group (95% CI 0.9 to 14.5 percentage points higher).

Figure 15. Forest plot of data by sample site

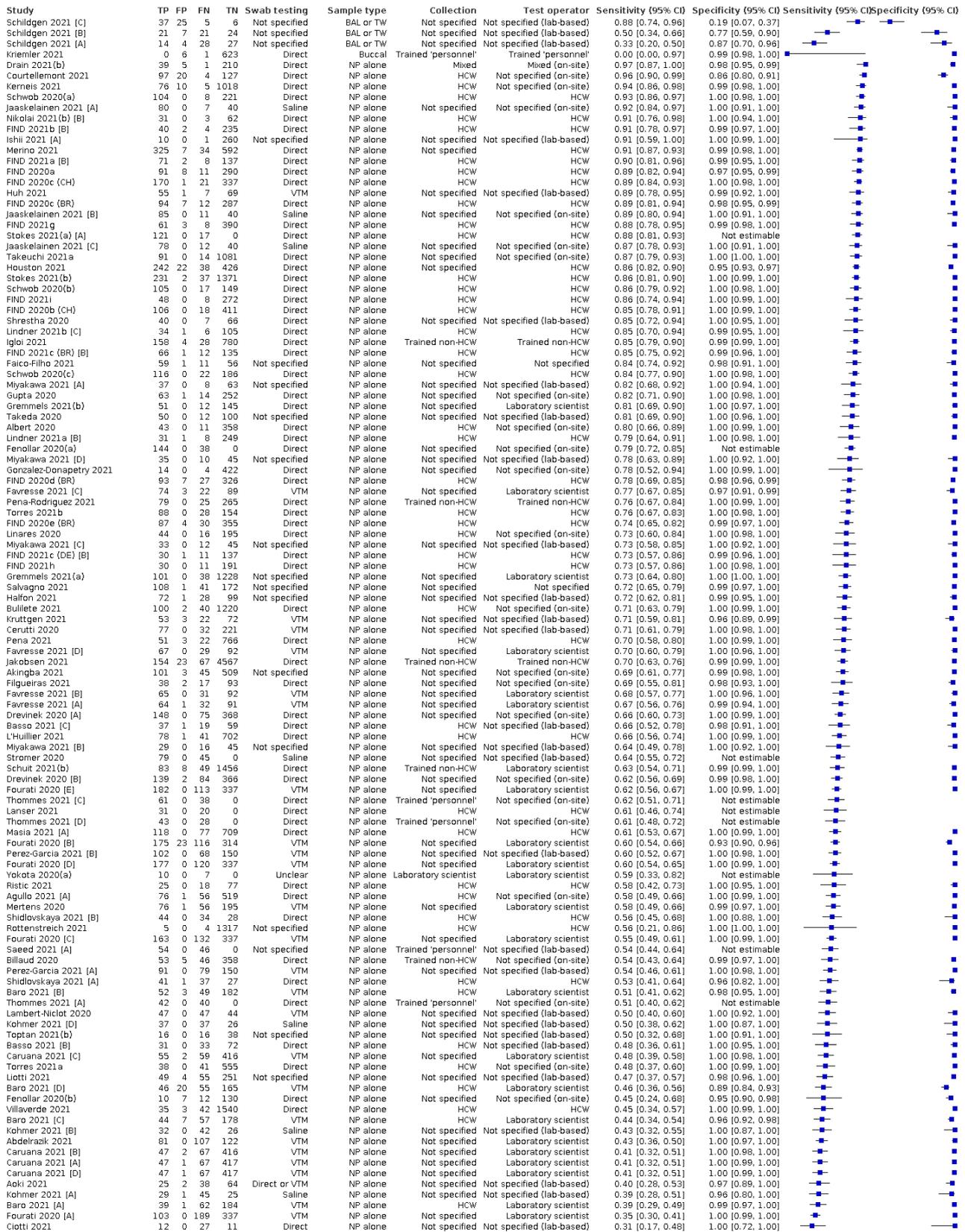


Figure 15. (Continued)

Agullo 2021 [C]	28	0	93	489	Direct	Saliva	Self-collected	Not specified (on-site)	0.23 [0.16, 0.32]	1.00 [0.99, 1.00]	■
Masia 2021 [C]	28	0	93	490	Direct	Saliva	Self-collected	HCW	0.23 [0.16, 0.32]	1.00 [0.99, 1.00]	■
Saeed 2021 [B]	21	0	79	0	Not specified	Saliva	Trained 'personnel'	Not specified (lab-based)	0.21 [0.13, 0.30]	Not estimable	■
Basso 2021 [A]	7	1	47	79	Direct	Saliva	Self-collected	Not specified (lab-based)	0.13 [0.05, 0.25]	0.99 [0.93, 1.00]	■
Nagura-Ikeda 2020	12	0	91	0	Direct	Saliva	Self-collected	Not specified (lab-based)	0.12 [0.06, 0.19]	Not estimable	■
Stokes 2021(a) [C]	1	0	40	0	Direct	Saliva	Self-collected	HCW	0.02 [0.00, 0.13]	Not estimable	■

In contrast however, the nine studies reporting within-participant comparisons of nasopharyngeal (2979 samples including 682 cases) and nasal samples (2710 samples including 619 cases) suggested no statistical evidence for a difference in sensitivity between sites (sensitivity was 2.9 percentage points lower in nasal samples compared to nasopharyngeal samples, 95% CI -16.1 to 10.4 percentage points; Table 2; Appendix 12 see Figure 16). Five of the nine studies reported the use of nasal sampling kit versions of the assays used (FIND 2021a [A]; FIND 2021b [A]; FIND 2021c (BR) [A];

FIND 2021c (DE) [A]; Nikolai 2021(b) [A]). No difference in specificity between nasopharyngeal and nasal sampling was observed overall (specificity 99.6% for both sample sites, 95% CI 99.2% to 99.8%) or in direct comparisons (specificity 99.6% for both sites, 95% CI 99.2% to 99.8%). When analysis was restricted to the six studies comparing nasopharyngeal and nasal mid-turbinate sampling, specificity was 2.0 percentage points lower for nasal mid-turbinate (95% CI from 1.3 to 2.7 percentage points lower, based on 1134 samples) (Table 2).

Figure 16. Forest plot of within-study comparisons by sample site, collection, or interpretation.

Study	TP	FP	FN	TN	Swab testing	Sample type	Collection	Test operator	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Agullo 2021 [A]	76	1	56	519	Direct	NP alone	HCW	Not specified (on-site)	0.58 [0.49, 0.66]	1.00 [0.99, 1.00]	■	■
Agullo 2021 [B]	59	0	73	527	Direct	Nasal (nos)	HCW	Not specified (on-site)	0.45 [0.36, 0.54]	1.00 [0.99, 1.00]	■	■
Agullo 2021 [C]	28	0	93	489	Direct	Saliva	Self-collected	Not specified (on-site)	0.23 [0.16, 0.32]	1.00 [0.99, 1.00]	■	■
Basso 2021 [A]	7	1	47	79	Direct	Saliva	Self-collected	Not specified (lab-based)	0.13 [0.05, 0.25]	0.99 [0.93, 1.00]	■	■
Basso 2021 [B]	31	0	33	72	Direct	NP alone	HCW	Not specified (lab-based)	0.48 [0.36, 0.61]	1.00 [0.95, 1.00]	■	■
FIND 2021a [A]	71	2	8	137	Direct	Nasal (NMT)	HCW	HCW	0.90 [0.81, 0.96]	0.99 [0.95, 1.00]	■	■
FIND 2021a [B]	71	2	8	137	Direct	NP alone	HCW	HCW	0.90 [0.81, 0.96]	0.99 [0.95, 1.00]	■	■
FIND 2021b [A]	38	2	6	235	Direct	Nasal (NMT)	HCW	HCW	0.86 [0.73, 0.95]	0.99 [0.97, 1.00]	■	■
FIND 2021b [B]	40	2	4	235	Direct	NP alone	HCW	HCW	0.91 [0.78, 0.97]	0.99 [0.97, 1.00]	■	■
FIND 2021c (BR) [A]	66	1	12	135	Direct	Nasal (NMT)	HCW	HCW	0.85 [0.75, 0.92]	0.99 [0.96, 1.00]	■	■
FIND 2021c (BR) [B]	66	1	12	135	Direct	NP alone	HCW	HCW	0.85 [0.75, 0.92]	0.99 [0.96, 1.00]	■	■
FIND 2021c (DE) [A]	33	1	8	137	Direct	Nasal (NMT)	HCW	HCW	0.80 [0.65, 0.91]	0.99 [0.96, 1.00]	■	■
FIND 2021c (DE) [B]	30	1	11	137	Direct	NP alone	HCW	HCW	0.73 [0.57, 0.86]	0.99 [0.96, 1.00]	■	■
Ishii 2021 [A]	10	0	1	260	Not specified	NP alone	Not specified	Not specified (lab-based)	0.91 [0.59, 1.00]	1.00 [0.99, 1.00]	■	■
Ishii 2021 [B]	3	0	6	84	Not specified	Saliva	Not specified	Not specified (lab-based)	0.33 [0.07, 0.70]	1.00 [0.96, 1.00]	■	■
Lindner 2021a [A]	29	2	10	248	Direct	Nasal (AN)	Self-collected	HCW	0.74 [0.58, 0.87]	0.99 [0.97, 1.00]	■	■
Lindner 2021a [B]	31	1	8	249	Direct	NP alone	HCW	HCW	0.79 [0.64, 0.91]	1.00 [0.99, 1.00]	■	■
Lindner 2021b [A]	33	0	7	104	Direct	Nasal (NMT)	Self-collected	Self-tested	0.82 [0.67, 0.93]	1.00 [0.97, 1.00]	■	■
Lindner 2021b [B]	34	0	6	105	Direct	Nasal (NMT)	Self-collected	HCW	0.85 [0.70, 0.94]	1.00 [0.97, 1.00]	■	■
Lindner 2021b [C]	34	1	6	105	Direct	NP alone	HCW	HCW	0.85 [0.70, 0.94]	0.99 [0.95, 1.00]	■	■
Masia 2021 [A]	118	0	77	709	Direct	NP alone	HCW	HCW	0.61 [0.53, 0.67]	1.00 [0.99, 1.00]	■	■
Masia 2021 [B]	59	0	73	527	Direct	Nasal (nos)	HCW	HCW	0.45 [0.36, 0.54]	1.00 [0.99, 1.00]	■	■
Masia 2021 [C]	28	0	93	490	Direct	Saliva	Self-collected	HCW	0.23 [0.16, 0.32]	1.00 [0.99, 1.00]	■	■
Nikolai 2021(a) [A]	31	0	5	96	Direct	Nasal (AN)	HCW	HCW	0.86 [0.71, 0.95]	1.00 [0.96, 1.00]	■	■
Nikolai 2021(a) [B]	31	0	5	96	Direct	Nasal (NMT)	HCW	HCW	0.86 [0.71, 0.95]	1.00 [0.96, 1.00]	■	■
Nikolai 2021(b) [A]	31	1	3	61	Direct	Nasal (NMT)	Self-collected	HCW	0.91 [0.76, 0.98]	0.98 [0.91, 1.00]	■	■
Nikolai 2021(b) [B]	31	0	3	62	Direct	NP alone	HCW	HCW	0.91 [0.76, 0.98]	1.00 [0.94, 1.00]	■	■
Saeed 2021 [A]	54	0	46	0	Not specified	NP alone	Trained 'personnel'	Not specified (lab-based)	0.54 [0.44, 0.64]	Not estimable	■	■
Saeed 2021 [B]	21	0	79	0	Not specified	Saliva	Trained 'personnel'	Not specified (lab-based)	0.21 [0.13, 0.30]	Not estimable	■	■
Stokes 2021(a) [A]	121	0	17	0	Direct	NP alone	HCW	HCW	0.88 [0.81, 0.93]	Not estimable	■	■
Stokes 2021(a) [B]	35	0	26	0	Direct	OP alone	HCW	HCW	0.57 [0.44, 0.70]	Not estimable	■	■
Stokes 2021(a) [C]	1	0	40	0	Direct	Saliva	Self-collected	HCW	0.02 [0.00, 0.13]	Not estimable	■	■

Overall, average sensitivities for studies using combined nasal and oropharyngeal samples, and in studies using nasopharyngeal samples in some but not all participants (e.g. sample site was either nasopharyngeal or oropharyngeal) were similar to results where nasopharyngeal samples were used in all participants (absolute differences of -0.3 and 2.9 respectively; Table 2). No direct comparisons of the accuracy of these sample sites were identified.

The number of evaluations contributing data to the primary analysis based on saliva or oropharyngeal samples alone was low (n = 4 and n = 2 respectively), however average sensitivities were lower than for nasopharyngeal or nasal samples, sensitivity 21.6% for saliva (95% CI 17.4% to 26.6%, based on 305 cases) and 57.4% for oropharyngeal samples (95% CI 26.6% to 83.4%, based on 214 cases). The four studies evaluating saliva samples also provided within-participant comparisons of accuracy with nasopharyngeal samples: the difference in sensitivity was 36.8 percentage points lower for saliva (95% CI from -43.5 to -30.1 percentage points). Adding data from two sensitivity-only cohorts increased the difference in sensitivity to 49.4 percentage points lower (sensitivity 66.5% for nasopharyngeal samples (95% CI 53.0% to 77.8%; based on 640 cases) and 17.1% for saliva (95% CI 10.1% to 27.5% based on 446 cases).

Two studies allowing a comparison of nasal (1318 samples) versus saliva samples (1221 samples), suggested higher sensitivity and similarly specificity from the use of nasal samples (Agullo 2021 [A]; Masia 2021 [A]), and one study also showed identical sensitivity and specificity in anterior nasal compared to nasal mid-turbinate (Nikolai 2021(a) [A]; Table 2; Appendix 12 see Figure 16).

Subgroup analyses including data from 'sensitivity-alone' evaluations produced similar average sensitivities and differences in sensitivity between sample types (Appendix 10).

Average specificities were greater than 99% for all of the main sample sites apart from in the 12 evaluations of either naso- or oropharyngeal samples where average specificity was 98.4% (95% CI 98.0% to 98.7%; Table 2).

Effect from test operator

Only one study directly compared the effect of assay interpretation by study participants compared to interpretation by a professional, both using nasal swabs (Lindner 2021b [A]); specificities were both 100% and sensitivity was 2.5 percentage points higher for the professional interpreted tests (85.0% compared to 82.5% for participant interpreted tests). The direction of effect is similar to

that observed in an indirect comparison by test operator from a PHE evaluation showing sensitivities of:

- 57.5% (95% CI 52.3% to 62.6%) when the test was used by self-trained, non-healthcare workers (n = 1; 372 cases; [Peto 2021\(b\) \[non-HCW tested\]](#));
- 70.0% (95% CI 63.5% to 75.9%) when the test was used by healthcare workers (n = 1; 223 cases; [Peto 2021\(c\) \[A - HCW tested\]](#)); and
- 78.8% (95% CI 72.4% to 84.3%) when the test was used by laboratory scientists (n = 1; 198 cases; [Peto 2021\(c\) \[A - Lab tested\]](#)).

Evaluations of accuracy in children

Restricting the analysis to the 10 evaluations reporting data for children in 4652 samples with 410 cases, average sensitivity was 62.7% (95% CI 52.7% to 71.7%) and average specificity 99.4% (95% CI 99.1% to 99.6%; [Table 2](#); [Figure 9](#)). Adding data from two sensitivity-only or one specificity-only evaluation had only a marginal effect on accuracy ([Table 2](#)).

Six evaluations allowed a comparison of results in children versus adults (so minimising the effect from other differences); average sensitivity was 9.9 percentage points higher (95% CI -8.7 to 28.4), and average specificity 0.7 percentage points higher (95% CI 0.2 to 1.2) in adults compared to children, however the number of SARS-

CoV-2 cases in children was relatively small and the difference for sensitivity was within that which might be observed by chance. These differences were maintained with the addition of data from two sensitivity-only evaluations and one specificity-only evaluation ([Table 2](#)).

Subgroup analysis by Ct value or RNA copies/mL

A total of 157 evaluations reported sensitivity according to sample viral load, either using PCR Ct values as a proxy, or by converting Ct values to RNA copies/mL which allows for a fairer comparison across studies using different RT-PCRs assays.

We first compared sensitivity above and below a single Ct or RNA copies/mL threshold to indicate higher or lower viral load. Results were very similar to those observed for the previous iteration of this review, with strong evidence for higher sensitivity in higher viral load subgroups ([Table 2](#); Appendix 12 see [Figure 17](#); [Figure 18](#); [Figure 19](#); [Figure 20](#); [Figure 21](#)). Because of the continuous nature of viral load measurement, and the lack of evidence for a step-change in RDT sensitivity above or below any single threshold value, we focus on presenting results for assay sensitivity in subgroups with smaller ranges in viral load. Results are reported in subgroups, firstly for studies reporting results according to Ct value and then for studies reporting results in RNA copies/mL ([Table 2](#); [Figure 10](#); [Figure 11](#)).

Figure 17. Forest plot of data in higher versus lower viral load subgroups (< or > 25 Ct). BR: Brazil; CH: Switzerland; Ct: cycle threshold; DE: Germany; HCW: healthcare worker

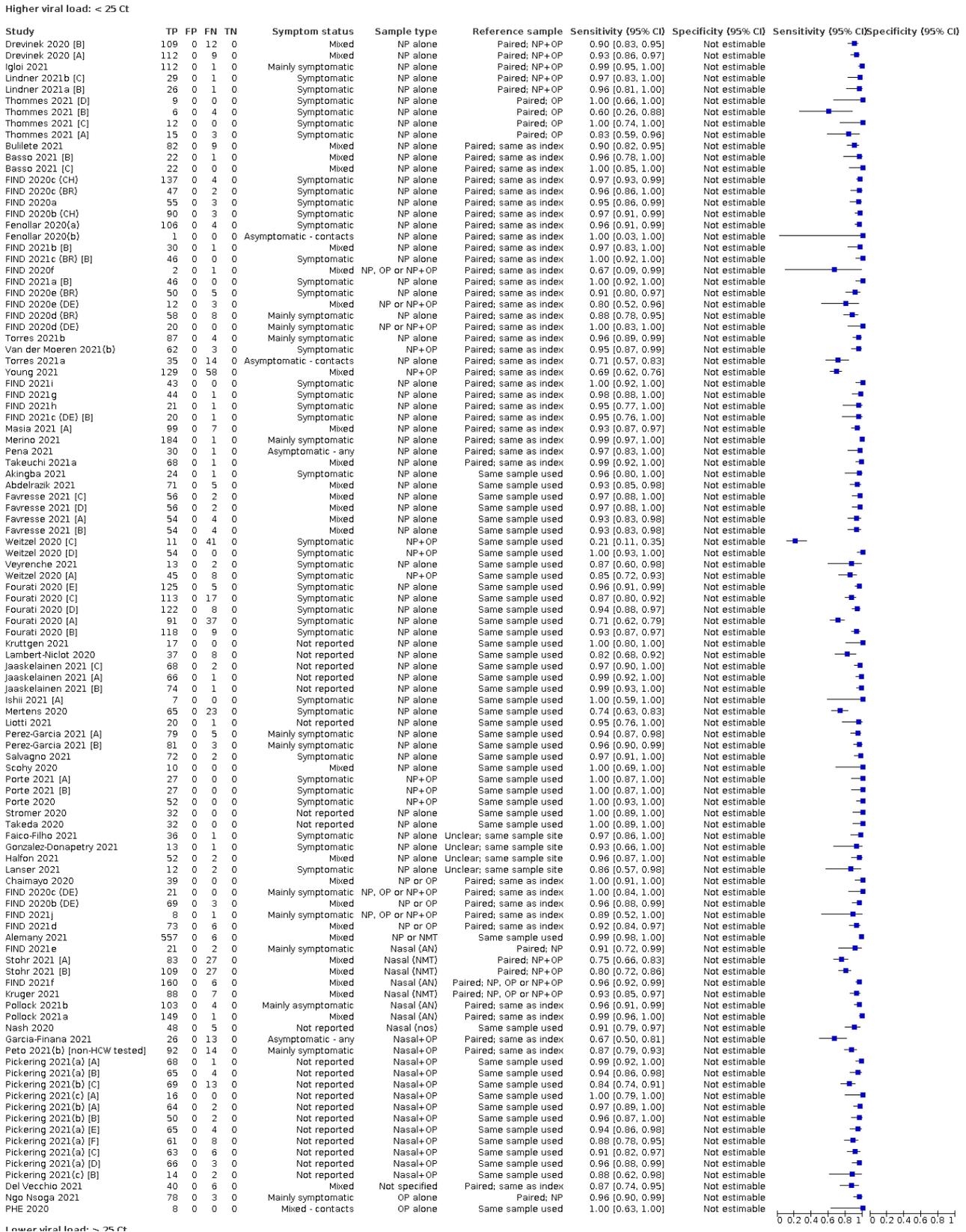


Figure 17. (Continued)

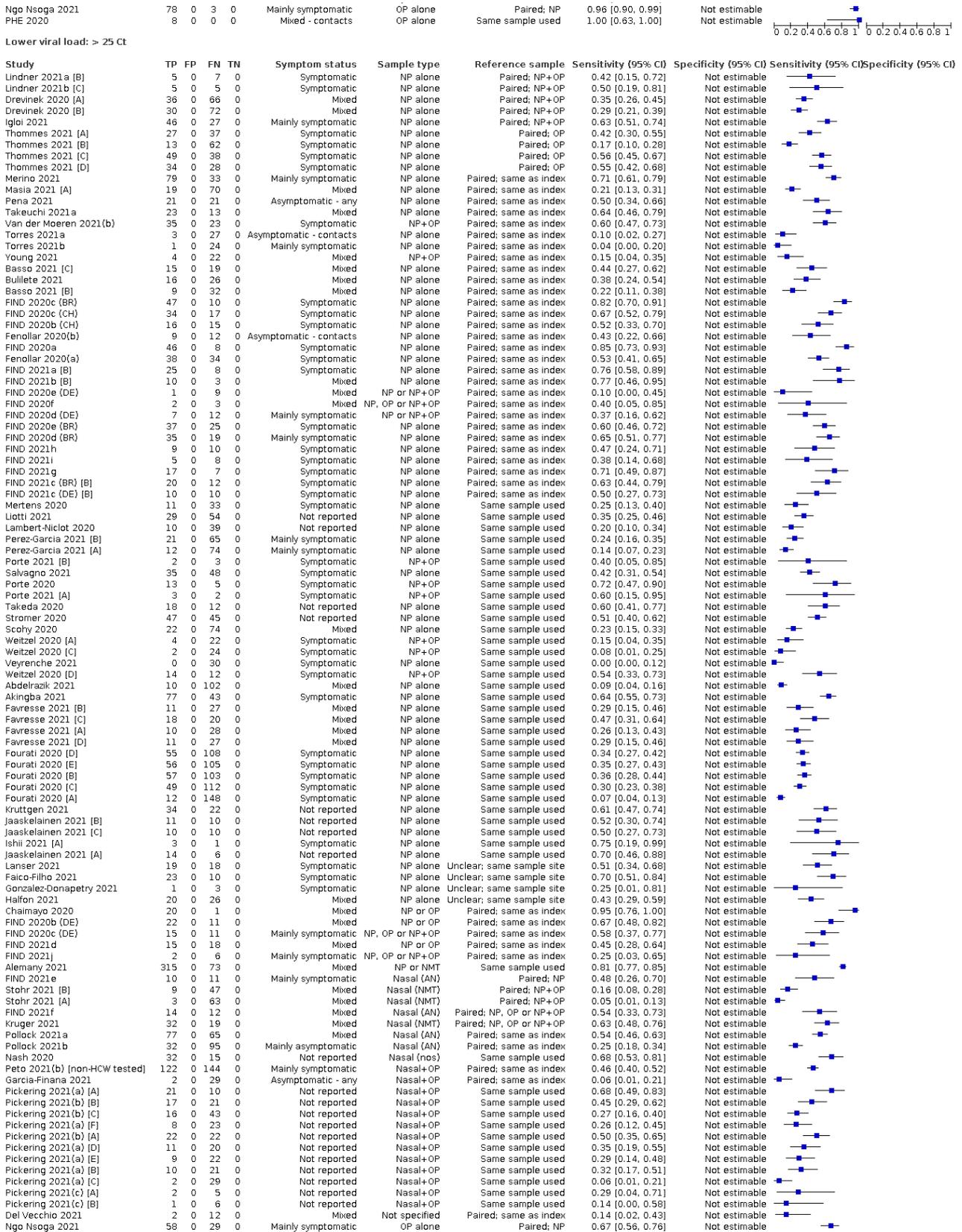


Figure 17. (Continued)

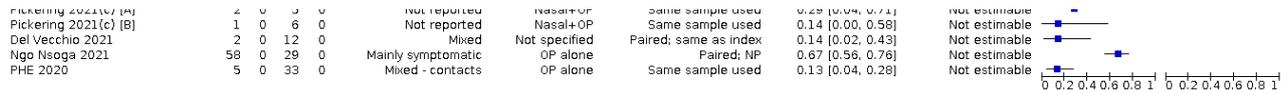


Figure 18. Forest plot of data in higher versus lower viral load subgroups (< or > 32/33 Ct threshold). BR: Brazil; CH: Switzerland; ; Ct: cycle threshold; DE: Germany

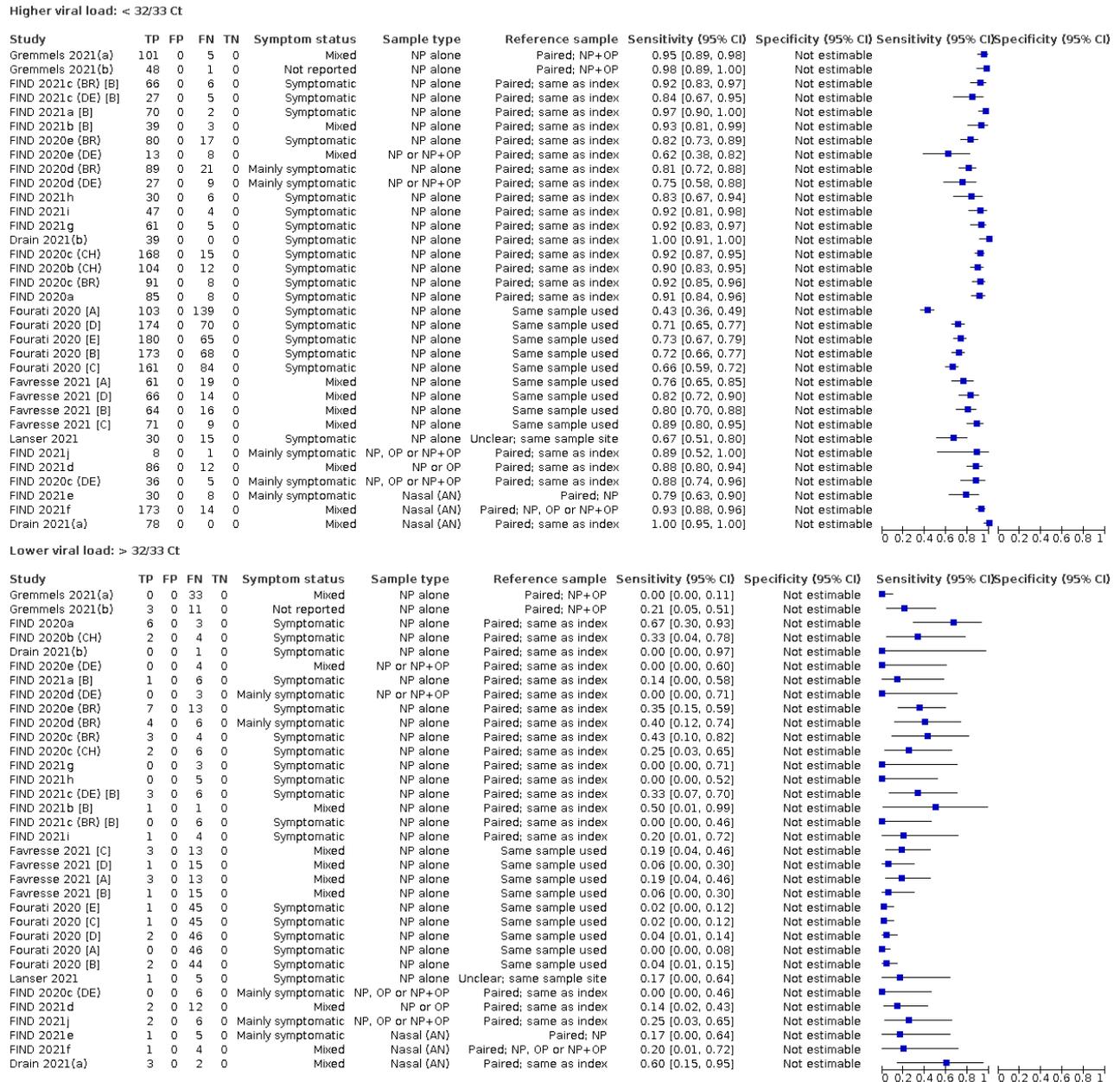
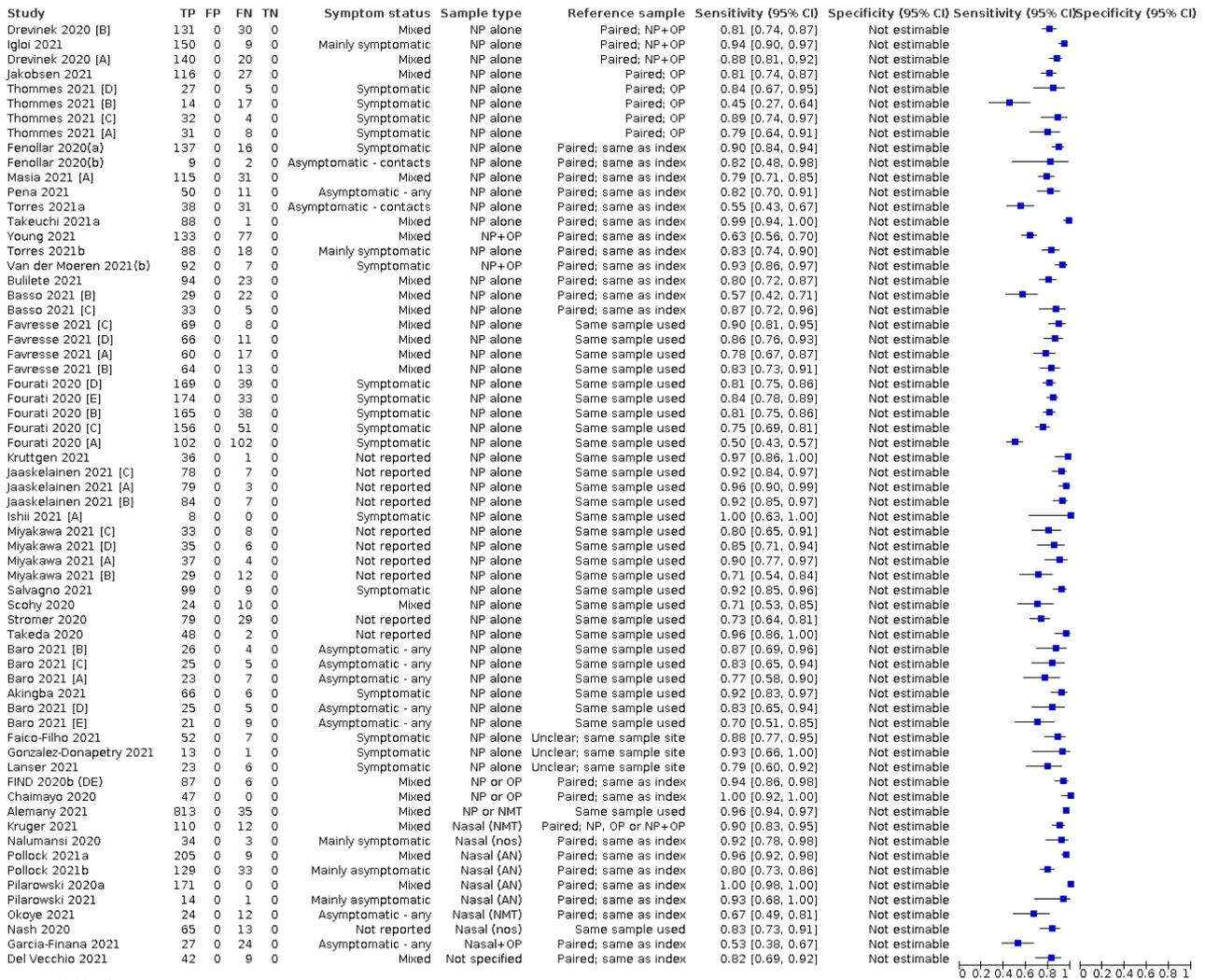


Figure 19. Forest plot of data in higher versus lower viral load subgroups (< or > 30 Ct). Ct: cycle threshold; HCW: healthcare worker

Higher viral load: < 30 Ct



Lower viral load: > 30 Ct

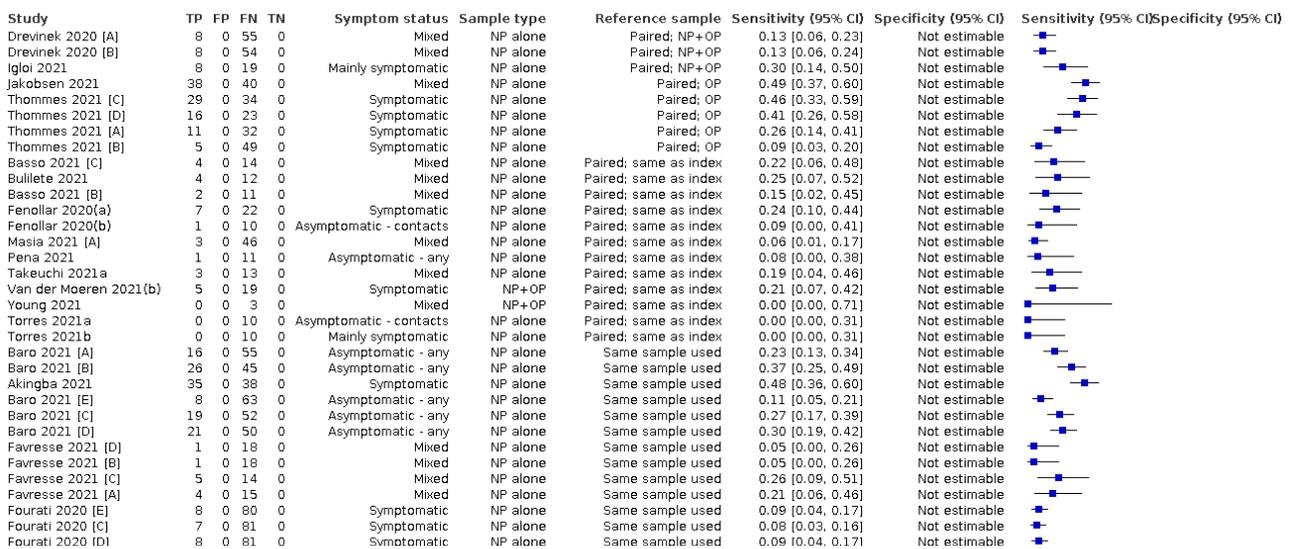


Figure 19. (Continued)

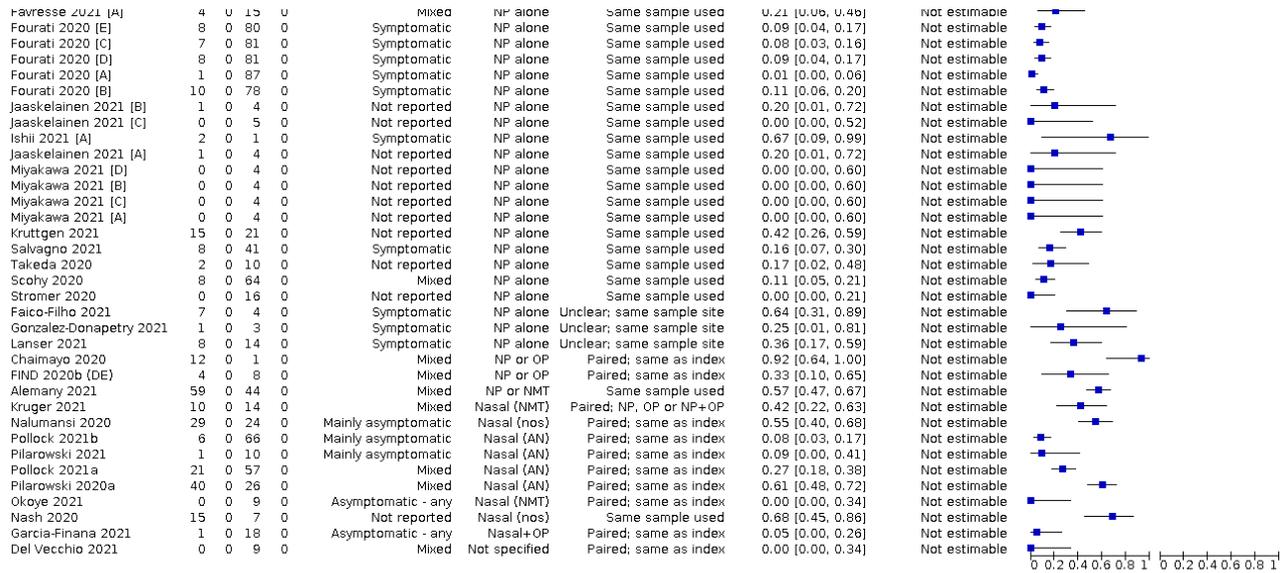


Figure 20. Forest plot of data in higher versus lower viral load subgroups (> or < 10⁶ RNA copies/mL)

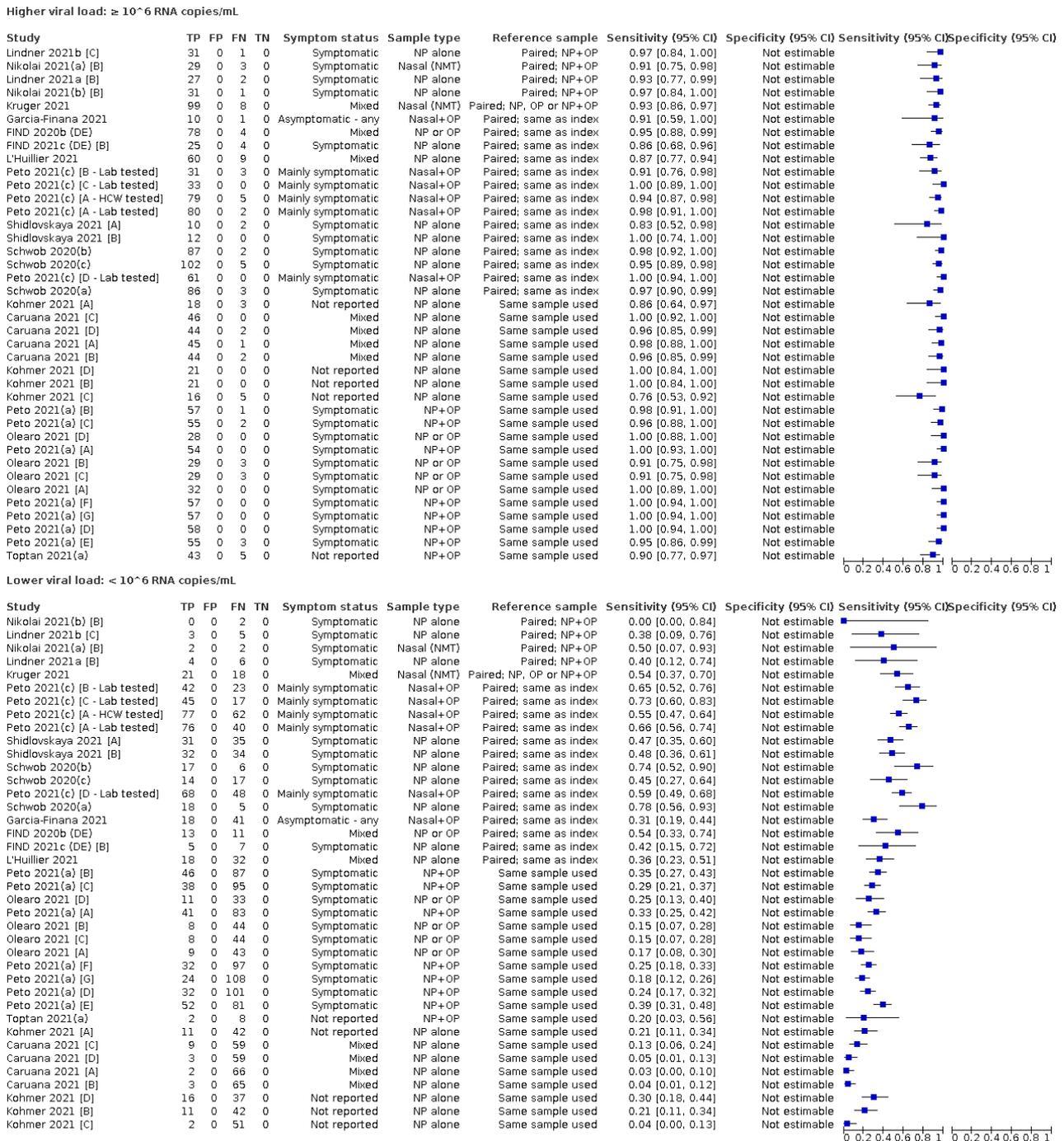
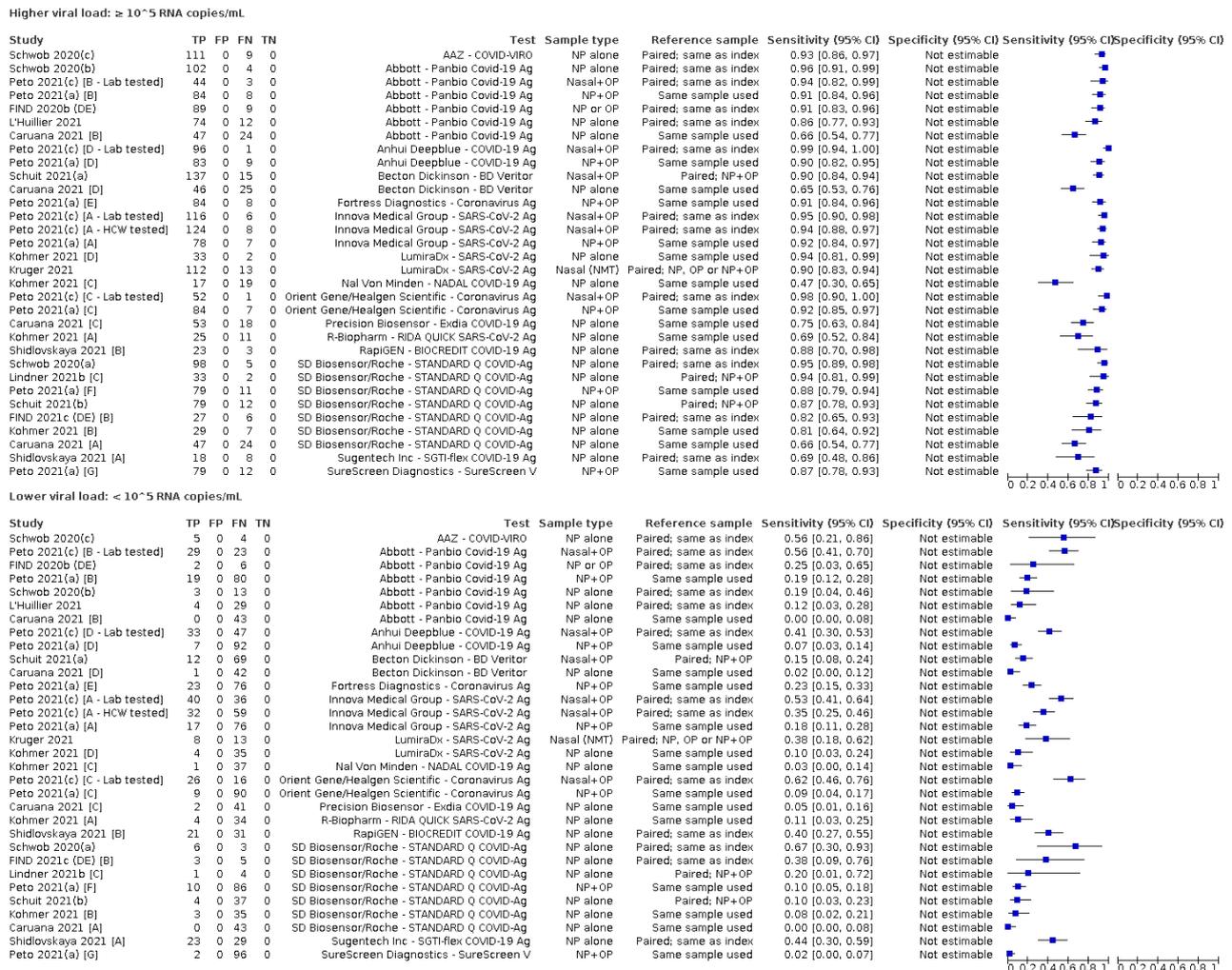


Figure 21. Forest plot of data in higher versus lower viral load subgroups (> or < 10⁵ RNA copies/mL)



For participant samples with the highest viral load, summary sensitivities were 97.4% for samples with Ct less than 20 (95% CI 95.0% to 98.6%; based on 26 evaluations including 1108 cases) and 98.4% for samples with 10⁷ RNA copies/mL or above (95% CI 97.0% to 99.1%; 21 evaluations, including 608 cases), respectively (Table 2). For those with Ct values in the 20 to 25 Ct range, or from 10⁶ to 10⁷ RNA copies/mL, summary sensitivities remained high: 93.6% (95% CI 90.0% to 96.0%; 27 evaluations, 1384 cases) and 94.0% (95% CI 89.8% to 96.6%; 28 evaluations, 597 cases). Summary sensitivities are considerably lower for samples in the 25 to 30 Ct or from 10⁵ to 10⁶ RNA copies/mL range, to 68.7% (95% CI 61.6% to 75.0%; 48 evaluations, 1724 cases) and 70.9% (95% CI 57.4% to 81.5%; 31 evaluations, 686 cases). Fewer evaluations reported results in the 30 to 35 Ct (n = 8) and greater than 35 Ct (n = 9) ranges, however the pattern of results was the same as for evaluations reporting results for samples with between 10⁴ and 10⁵ RNA copies/mL, or with less than 10⁴ RNA copies/mL, where average sensitivities were 36.7% (95% CI 24.7% to 50.5%; 24 evaluations, 582 cases) and 7.5% (95% CI 3.8% to 14.3%; 24 evaluations, 825 cases), respectively (Table 2). Average sensitivity from evaluations reporting results for samples with Ct values

greater than 30 Ct were 18.7% (95% CI 14.2% to 24.1%), based on 2332 cases.

Subgroup analysis by assay format

We found some evidence for differences in accuracy according to assay format (Table 2). Average sensitivity was lower for evaluations using a CGIA at 68.5% (95% CI 65.1% to 71.7%; 140 evaluations; 95,926 samples, 17146 cases) compared to FIA (average sensitivity 76.6%, 95% CI 68.2% to 83.4%; n = 19, 6987 samples, 1507 cases). The absolute difference in average sensitivities was 8.2 percentage points (95% CI -0.1 to 16.5 percentage points). Average specificities were 99.4% (95% CI 99.3% to 99.4%) for CGIAs and 97.5% (95% CI 97.1% to 97.9%) for FIAs; a difference of -1.9 percentage points (95% CI -2.3 to -1.4 percentage points). Results for LFAs where the method could not be determined (n = 12) and for alkaline phosphatase (ALP)-labelled assays were lower than those observed for the other assay types (Table 2). Average sensitivities for latex-conjugated LFAs (2 evaluations in 2048 samples, 156 cases) and microfluidic fluorescent immunoassays (4 evaluations in 1373 samples, 343 cases) were higher, 81.3% (95% CI 69.9% to 89.0%) and 89.7% (95% CI 63.0% to 97.8%), respectively.

Results by test brand according to symptom status and IFU compliance

In contrast to the previous iteration of this review we focus on results by test brand according to symptom status (i.e. using separate summary results for $\geq 75\%$ symptomatic or $\geq 75\%$ asymptomatic populations) with sensitivity analyses by IFU compliance (based on sample type, use of VTM, and time period between sample collection and test procedure). Summary results by brand are presented in [Table 3](#) and [Figure 12](#) (showing results per study if only one study per brand). [Figure 13](#) shows individual

study results for the 23 studies reporting within-study comparisons of test brands; summary results are reported in [Table 4](#).

Forest plots of individual study data are in Appendix 13, see [Figure 22](#) (all data regardless of symptoms), [Figure 23](#) (symptomatic), [Figure 24](#) (asymptomatic). Overall results by test brand (regardless of symptom status) and sensitivity analyses by IFU compliance are reported in Appendix 14. An overall summary of results is provided below, and a detailed synthesis of results by test brand is reported in Appendix 15.

Figure 22. Forest plot of individual study results overall (regardless of symptom status) by assay

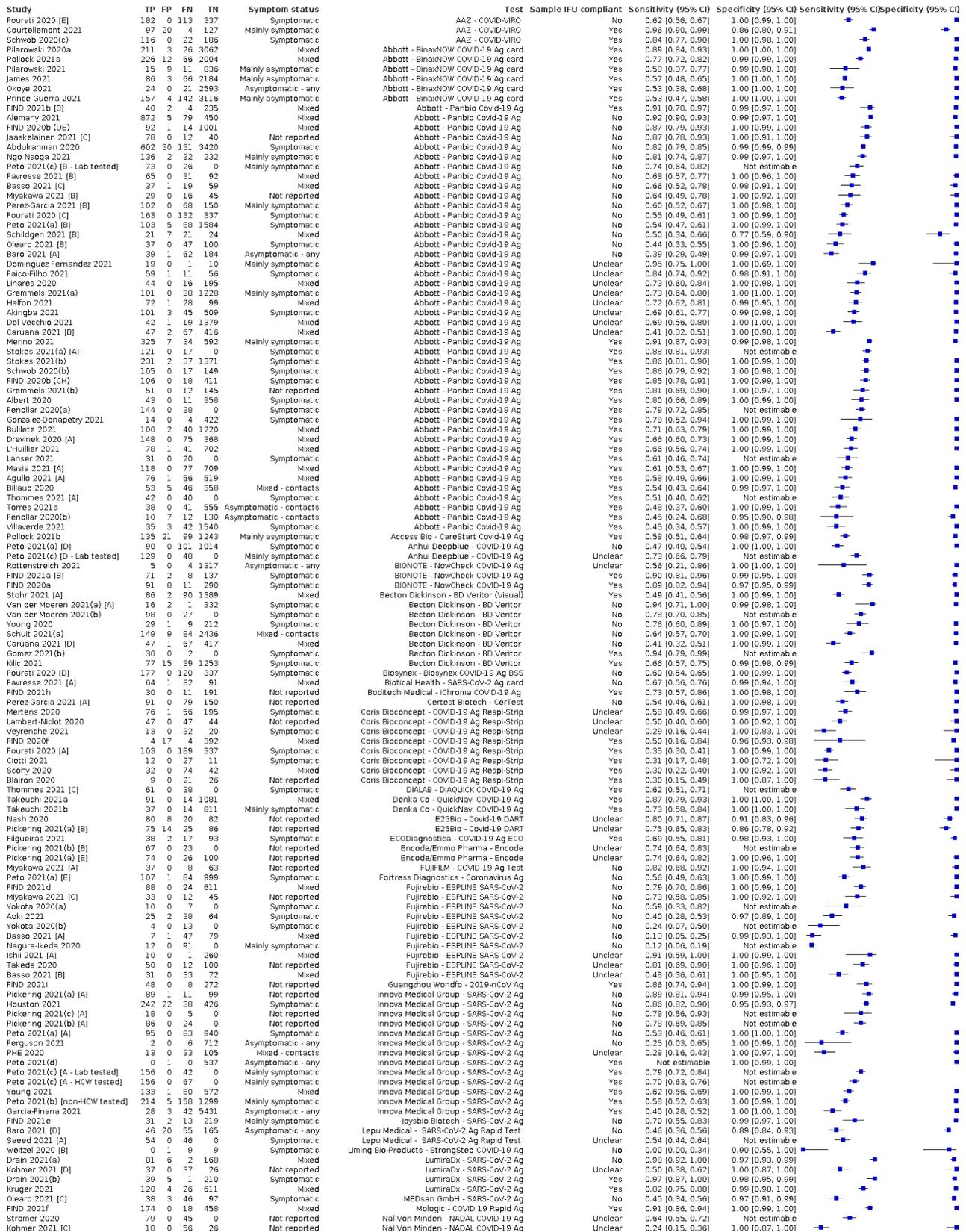


Figure 22. (Continued)

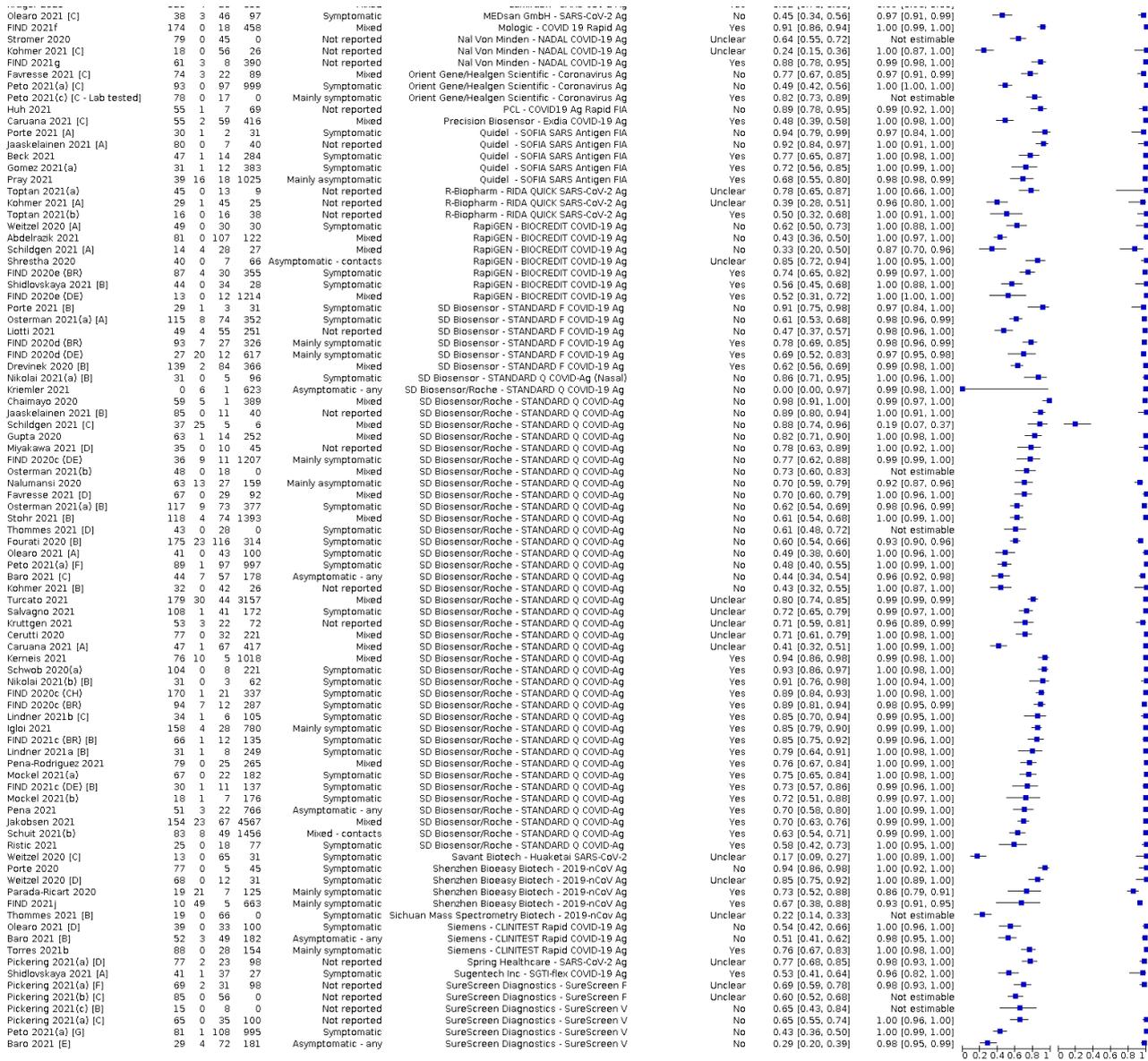


Figure 23. Forest plot of individual study results in symptomatic participants by assay

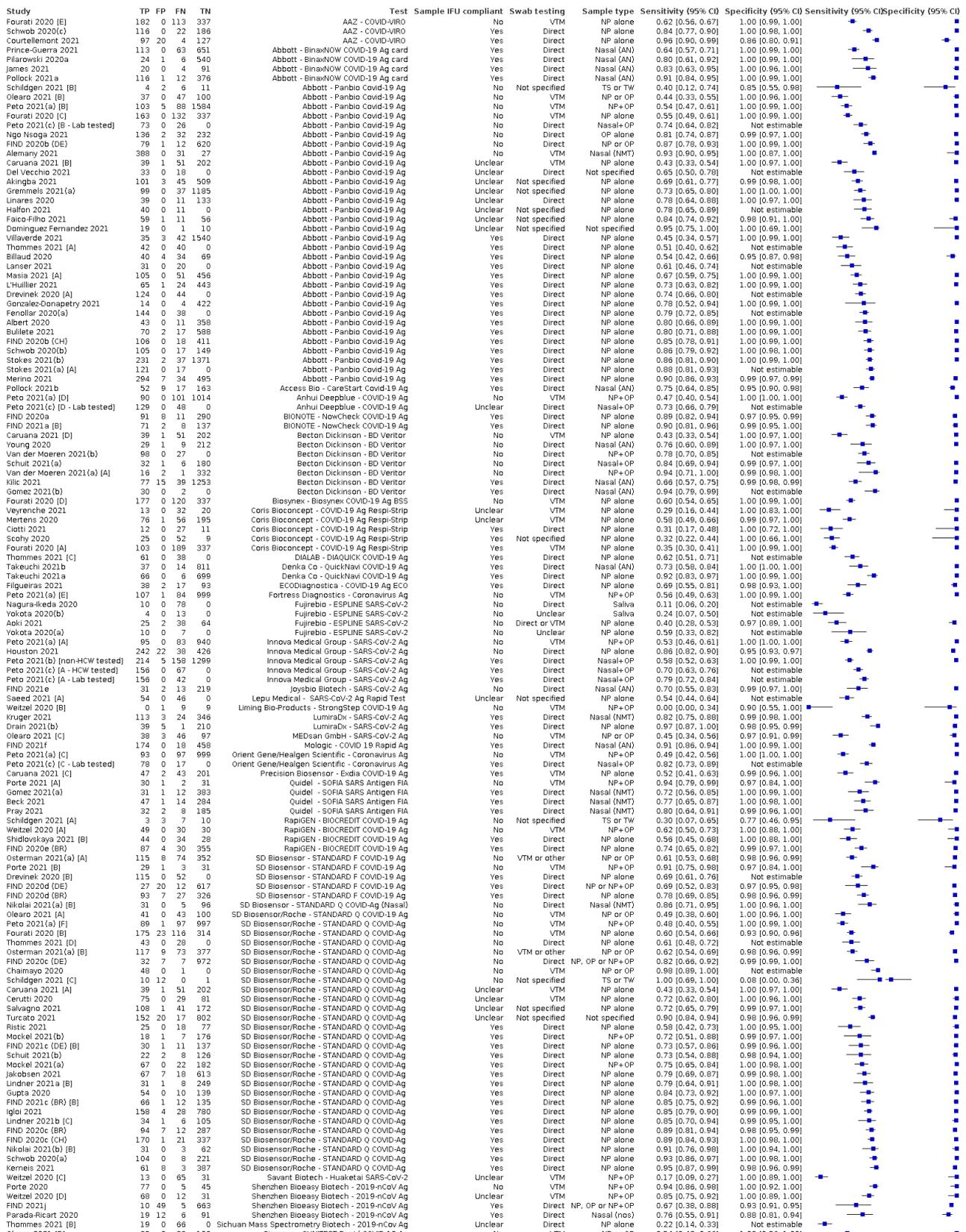


Figure 23. (Continued)

Weitzel 2020 [D]	68	0	12	31	Shenzhen Bioeasy Biotech - 2019-nCoV Ag	Unclear	VTM	NP+OP	0.85 [0.75, 0.92]	1.00 [0.99, 1.00]	
FIND 2021j	10	49	5	663	Shenzhen Bioeasy Biotech - 2019-nCoV Ag	Yes	Direct	NP, OP or NP+OP	0.67 [0.38, 0.88]	0.93 [0.91, 0.95]	
Parada-Ricart 2020	19	12	6	91	Shenzhen Bioeasy Biotech - 2019-nCoV Ag	Yes	Direct	Nasal (nos)	0.76 [0.55, 0.91]	0.88 [0.81, 0.94]	
Thommes 2021 [B]	19	0	66	0	Siichuan Mass Spectrometry Biotech - 2019-nCoV Ag	Unclear	Direct	NP alone	0.22 [0.14, 0.33]	Not estimable	
Oleaso 2021 [D]	39	0	33	100	Siemens - CLINITEST Rapid COVID-19 Ag	No	VTM	NP or OP	0.54 [0.42, 0.66]	1.00 [0.96, 1.00]	
Torres 2021b	73	0	18	87	Siemens - CLINITEST Rapid COVID-19 Ag	Yes	Direct	NP alone	0.80 [0.71, 0.88]	1.00 [0.96, 1.00]	
Shidlovskaya 2021 [A]	41	1	37	27	Sugentech Inc - SGT-flex COVID-19 Ag	Yes	Direct	NP alone	0.53 [0.41, 0.64]	0.96 [0.82, 1.00]	
Peto 2021(a) [G]	81	1	108	995	SureScreen Diagnostics - SureScreen V	No	VTM	NP+OP	0.43 [0.36, 0.50]	1.00 [0.99, 1.00]	

Figure 24. Forest plot of individual study results in asymptomatic participants by assay

Study	TP	FP	TN	FN	Test	Sample IFU compliant	Swab testing	Sample type	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Prince-Guerra 2021	44	4	79	2465	Abbott - BinaxNOW COVID-19 Ag card	Yes	Direct	Nasal (AN)	0.36 [0.27, 0.45]	1.00 [1.00, 1.00]		
James 2021	66	3	62	2093	Abbott - BinaxNOW COVID-19 Ag card	Yes	Direct	Nasal (AN)	0.52 [0.43, 0.60]	1.00 [1.00, 1.00]		
Okoye 2021	24	0	21	2593	Abbott - BinaxNOW COVID-19 Ag card	Yes	Direct	Nasal (NMT)	0.53 [0.38, 0.68]	1.00 [1.00, 1.00]		
Pilarowski 2021	15	9	11	836	Abbott - BinaxNOW COVID-19 Ag card	Yes	Direct	Nasal (AN)	0.58 [0.37, 0.77]	0.99 [0.98, 1.00]		
Pollock 2021a	110	11	54	1628	Abbott - BinaxNOW COVID-19 Ag card	Yes	Direct	Nasal (AN)	0.67 [0.59, 0.74]	0.99 [0.99, 1.00]		

Comparisons by brand in symptomatic populations

A total of 33 test brands were evaluated in symptomatic or mainly symptomatic participants (n = 132 evaluations, including 24 in sensitivity-only cohorts). Evaluations of the nasal kit versions of two brands (BIONOTE Nowcheck and SD Biosensor STANDARD Q) were considered separately and are also reported in Table 3. We observed considerable heterogeneity in sensitivities for almost all assays (Appendix 13).

Twelve test brands were evaluated in three or more evaluations (total of 105 evaluations) and we meta-analyzed results using the bivariate model (Figure 12). Six test brands were evaluated in two evaluations each and we therefore meta-analysed them using univariate analysis or by summing 2x2 tables (assays from Anhui Deepblue, BIONOTE, Denka Co, LumiraDx, Orient Gene and Siemens).

For test brands with three or more studies, the total number of samples per assay ranged from 251 for the Fujirebio assay to 15,331 for Abbott Panbio, and number of cases from 123 for Denka QuickNavi to 3989 for Abbott Panbio. Fifteen test brands were evaluated in a single evaluation each, with between 19 (Liming assay) and more than 1000 samples (SureScreen V assay and

Fortress Diagnostics), and between nine (Liming assay) and 297 (Biosynex assay) samples from SARS-CoV-2-positive cases. Average sensitivities ranged from 29.6% (95% CI 14.6% to 51.0%) for the Fujirebio assay based on 251 samples and 185 cases) to 91.2% (95% CI 70.0% to 97.9%) for LumiraDx, based on 741 samples and 177 cases). Specificities ranged from 93.2% (95% CI 91.3% to 94.6%) for the Shenzhen Bioeasy assay (n = 4, 1093 samples including 202 cases) to 100% (Anhui Deepblue, Denka QuickNavi, Orient Gene assay and Siemens CLINITEST) (Figure 12).

Using all data in symptomatic people, based on meta-analyses, only the seven assays from AAZ, Abbott BinaxNOW, BIONOTE, Denka QuickNavi, LumiraDx, Quidel, and Shenzhen Bioeasy met the WHO threshold for acceptable sensitivity (point estimate for sensitivity of 80% or more), and only the LumiraDx assay exceeded the desirable sensitivity target of 90%. Of these, all except the Shenzhen Bioeasy assay met acceptable specificity levels (point estimate of 97% or more).

We judged just over half of evaluations (70/132) to be compliant with manufacturer IFUs in terms of sample site, use of VTM and time between sample collection and testing. Based on meta-analyses, only five assays met the WHO acceptable performance

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

standards for both sensitivity and specificity based on IFU-compliant evaluations:

- Abbott - BinaxNOW COVID-19 Ag card: 80.9% (95% CI 67.6% to 89.6%) and 99.9% (95% CI 99.5% to 100%); n = 4 evaluations, 2018 samples including 358 cases ([James 2021](#); [Pilarowski 2020a](#); [Pollock 2021a](#); [Prince-Guerra 2021](#));
- BIONOTE – NowCheck: 89.5% (95% CI 84.1% to 93.2%) and 97.7% (95% CI 95.8% to 98.8%); n = 2, 618 samples, 181 cases ([FIND 2020a](#); [FIND 2021a \[B\]](#));
- Denka Co – QuickNavi: 84.2% (95% CI 66.2% to 93.5%) and 100% (95% CI 99.8% to 100%); n = 2 evaluations, 1633 samples, 123 cases ([Takeuchi 2021a](#); [Takeuchi 2021b](#));
- LumiraDx: 91.2% (95% CI 70.0% to 97.9%) and 98.6% (95% CI 97.2% to 99.3%); n = 2, 741 samples, 177 cases ([Drain 2021\(b\)](#); [Kruger 2021](#));
- SD Biosensor/Roche - STANDARD Q COVID-Ag: 84.0% (95% CI 79.2% to 87.9%) and 99.2% (95% CI 98.8% to 99.4%); n = 15; 5116 samples, 1197 cases ([FIND 2020c \(BR\)](#); [FIND 2020c \(CH\)](#); [FIND 2021c \(BR\) \[B\]](#); [FIND 2021c \(DE\) \[B\]](#); [Igloi 2021](#); [Jakobsen 2021](#); [Kerneis 2021](#); [Lindner 2021a \[B\]](#); [Lindner 2021b \[C\]](#); [Mockel 2021\(a\)](#); [Mockel 2021\(b\)](#); [Nikolai 2021\(b\) \[B\]](#); [Ristic 2021](#); [Schuit 2021\(b\)](#); [Schwob 2020\(a\)](#)).

Point estimates for sensitivity and specificity for a further two assays met WHO acceptable or desirable standards in a single evaluation each:

- Mologic - COVID 19 Rapid Ag: (sensitivity 90.6%, 95% CI 85.6% to 94.3% and specificity 100% (95% CI 99.2, 100; based on 650 samples including 192 cases ([FIND 2021f](#));
- Siemens – CLINITEST: 80.2% (95% CI 70.6% to 87.8%) and 100% (95% CI 95.8% to 100%); n = 1, 178 samples with 91 cases ([Torres 2021b](#)).

Note that for the majority of assays, the lower bound of the 95% CI for sensitivity does not exceed 80%, reflecting considerable remaining variability between studies even after restricting to those judged to meet IFU requirements.

For the two assays with evaluations carried out using nasal sampling kits, BIONOTE NowCheck (n = 1) and SD Biosensor STANDARD Q (n = 4), similar results to those using nasopharyngeal sampling kits were observed ([Table 3](#)).

Comparisons by brand in asymptomatic populations

A total of 19 test brands were evaluated in asymptomatic or mainly asymptomatic participants (n = 56 evaluations, including 6 in sensitivity-only cohorts). We observed considerable heterogeneity in sensitivities for all assays ([Appendix 13](#)).

Three test brands (Abbott BinaxNOW, Abbott Panbio and SD Biosensor STANDARD Q) were evaluated in three or more evaluations (total of 36 evaluations) and we meta-analysed results using the bivariate model ([Figure 13](#)). Four test brands were evaluated in two evaluations each and we meta-analysed them using univariate analysis or by summing 2x2 tables (assays from Becton Dickinson, Innova Medical Group, RapiGEN, and Siemens). The total number of samples per assay ranged from 140 (RapiGEN, including 60 cases) to 12,530 (Abbott BinaxNOW, 588 cases). A further 12 test brands were evaluated in a single evaluation each, with between 15 (Fujirebio assay) and 1326 samples (BIONOTE - NowCheck), and between one (Shenzhen Bioeasy assay) and 165 cases (Access Bio).

None of the assays met the WHO acceptable performance standard for sensitivity (of 80%) either based on meta-analysis or in individual studies in asymptomatic people. Average sensitivities ranged from 38.5% (95% CI 28.4% to 49.7%; Innova assay; n = 2 including 6224 samples and 78 cases) to 63.2% (95% CI 21.7% to 91.4%; RapiGen; n = 2, 140 samples and 60 cases) and average specificities from 98.8% (95% CI 91.7% to 99.8%; RapiGen) to 100% (95% CI 99.8% to 100%; Innova assay; [Figure 13](#)). The highest observed sensitivities in individual studies (both compliant with manufacturer IFUs) were:

- Denka Co QuickNavi: 75.8% (95% CI 57.7% to 88.9%) and 100% (95% CI 99.0% to 100%); 415 samples including 33 cases ([Takeuchi 2021a](#));
- LumiraDx assay: 77.8% (95% CI 40.0% to 97.2%) and 99.6% (95% CI 97.9% to 100%); 272 samples and 9 cases ([Kruger 2021](#)).

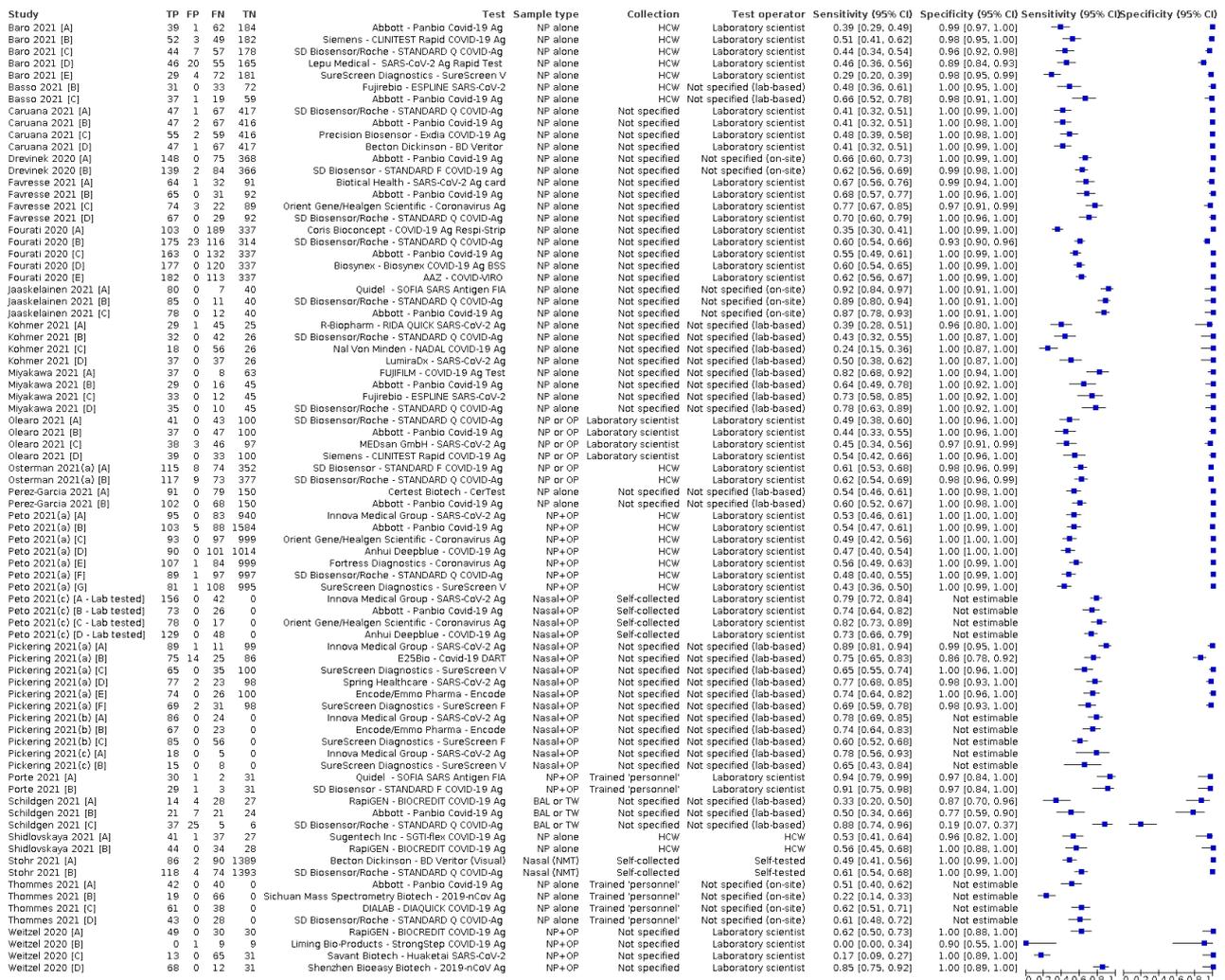
We judged just over half of evaluations (28/56) to be compliant with manufacturer IFUs in terms of sample site, use of VTM and time between sample collection and testing. On an individual study level, three of the 13 assays met the WHO acceptable sensitivity standard of 80% or more (Abbott Panbio, Abbott BinaxNOW and SD Biosensor STANDARD Q in one evaluation each, with case numbers ranging from 17 to 102). However, the average sensitivities for these assays ranged from 57.9% (95% CI 35.4% to 77.5%; Abbott Panbio; n = 7; 2502 samples and 279 cases) to 64.6% (95% CI 51.3% to 75.9%; SD Biosensor STANDARD Q; n = 4; 5914 samples and 250 cases).

Specificities were 99% or higher (meeting WHO acceptable performance standard for specificity) for 9 of 13 assays with IFU-compliant evaluations ([Table 3](#)).

Direct test comparisons

A total of 23 studies provided within-study comparisons by test brand ([Appendix 13](#) see [Figure 25](#)): 19 reported both sensitivity and specificity data, and four were sensitivity-only cohorts. Less than half of studies had sufficient assay comparisons in common to allow formal direct comparison using meta-analysis ([Table 4](#)).

Figure 25. Forest plot of data from studies reporting within-study comparisons by test brand



at T2. The specificity of the STANDARD Q assay was 98.9% (95% CI 97.7% to 99.6%) at T1 and 99.5% (95% CI 98.7% to 99.9%) at T2.

A second study evaluated weekly testing using the Abbott Panbio assay in football players, staff and referees from 13 professional football clubs and the national teams in the Netherlands over a five- to six-week period (Winkel 2020). Results from symptomatic participants at the time of testing were excluded from the study. A total of 824 people provided 2425 paired nasopharyngeal (for RDT) and naso- and oropharyngeal (for PCR) samples that were collected and tested on site by trained personnel; 52 individuals were positive on RT-PCR (68 samples), 23 (44%) of whom remained asymptomatic during the testing period and 29 developed symptoms after the positive PCR result. Results were available only on a per sample basis but were separated according to phase of infection (Table 5). The observed sensitivity of the RDT was 90% or higher during the pre-symptomatic and early infection phases: 91.7% (95% CI 61.5% to 99.8%; based on 12 PCR-positive samples) and 90.6% (95% CI 75.0% to 98.0%; based on 32 PCR-positive samples). Seven days after first positive PCR or after symptom onset (late infection), sensitivity fell to 33.3% (95% CI 14.6% to 57.0%; based on 21 samples) and to 0% (based on 3 samples) four weeks after first positive PCR. Specificity (on a per sample basis) was 99.5% (95% CI 99.2% to 99.8%; 11 RDT-positive samples from a total of 2338 PCR negative).

Two studies evaluated daily RDT testing. Love 2021 was a UK feasibility study of daily testing of contacts of confirmed SARS-CoV-2 cases to allow release from self-isolation, Smith 2021 evaluated daily testing of PCR-positive students in the USA and their contacts to determine the sensitivity of RDT, direct saliva RT-PCR and conventional RT-PCR using nasal swabs over time.

In Love 2021, samples were self-collected and self-tested with the RDT. At least one RDT and one PCR result were available for 346 participants out of the 812 who were sent a test kit (PCR was required either if the daily RDT was positive or at the end of the seven-day testing period), including only 55 of the 102 who reported at least one positive RDT. Overall sensitivity of was 82.8% (95% CI 71.3% to 91.1%; based on 64 SARS-CoV-2-positive on PCR) and specificity was 99.3% (95% CI 97.5% to 99.9%; based on 282 with negative PCR results; Table 5). The majority of cases were in those who self-reported as having developed symptoms of COVID-19 (55/346 participants, including 45 PCR-positive cases); RDT sensitivity was 88.9% (95% CI 75.9% to 96.3%; based on 45 cases) and specificity 80.0% (95% CI 44.4% to 97.5%; based on 10 PCR-negative participants). In those who remained asymptomatic and who returned RDT and PCR results (291/346, 84%), sensitivity was 68.4% (95% CI 43.4% to 87.4%; 19 PCR positive) and specificity was 100% (95% CI 98.7% to 100%; 272 PCR-negative participants). PCR Ct values for samples from the 11 false-negative cases ranged from 16.9 to 33.5 Ct (median 24.0)

Smith 2021 reported results for 43 of 51 PCR-positive individuals who had positive results on viral culture. Participants were enrolled either within 24 hours of a positive PCR result from routine surveillance or as contacts of a PCR-positive individual. Participants self-collected samples for daily testing with Quidel's SOFIA assay (nasal swabs), direct RT-PCR (saliva) and conventional PCR (nasal swabs). All testing was laboratory-based and was conducted within a day of sample collection. The testing of contacts allowed the study authors to calculate assay sensitivity in relation to the time before or after the first successful culture

(reported as the 'daily sensitivity' of the RDT and both PCRs). Only around a quarter (10 participants for 2 days prior to positive viral culture) to a half (20 participants for 1 day prior) of participants reported results for samples collected before successful viral culture, however results suggest that both PCR-based approaches were considerably more sensitive (between 70% and 80% sensitive) than testing using the RDT (30% sensitive at two days prior and 40% sensitive the day before positive viral culture; Table 5). For samples collected on the day that viral culture became positive, RDT sensitivity increased to 90.5% (based on 42 samples), compared to 97.6% for direct saliva PCR and 100% for conventional PCR. Daily sensitivity increased slightly for the RDT and direct PCR assays using samples collected on the following day ($n = 43$), sensitivities 97.7%, 100% and 95.3%, and then began to decline a faster rate for the RDT compared to the other assays. By day 4 after positive viral culture, the RDT daily sensitivity (based on 43 samples) was 62.8% compared to 95.3% for direct PCR and 43% for conventional PCR (Table 5). The study authors used daily sensitivity results to model the probability of a positive result before or during the period when viral culture is positive for testing strategies using each assay; sensitivities were highest for a PCR-based approach, however differences were relatively small (Table 5).

DISCUSSION

This is the third iteration of a Cochrane living review summarising the accuracy of point-of-care antigen tests for detecting current SARS-CoV-2 infection. This version of the review is based on published journal articles or studies available as preprints from 1 January 2020 up until 9 March 2021. 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 to 30 April 2021.

Summary of main results

We included data from 152 studies evaluating the accuracy of a single antigen test application, including 100,462 participants (16,822 samples with confirmed SARS-CoV-2), and four studies evaluating the accuracy of repeated test applications (1920 participants, 160 with confirmed SARS-CoV-2). The main results focus on the former group of studies reporting evaluations of a single antigen test application; these report a total of 210 test evaluations and a further 18 evaluations comparing accuracy in different sample sites. Key findings are presented in the Summary of findings 1.

Key findings

We summarize eight key findings from this review.

1. Lack of evidence for commercially produced tests

Despite a considerable increase in the number of studies evaluating point-of-care antigen tests, we did not identify any published or preprint reports of accuracy for a significant proportion of commercially produced point-of-care tests. This review located evaluations for 49 RDTs; these represent a small proportion of the 321 commercially produced assays (FIND 2022a).

2. Methodological standards have improved

Some improvements in methodological standards can be observed for antigen test evaluations compared to those in the previous

version of this review, particularly in regard to the applicability of the evidence for both the participant selection domain and the index test domain, with tests increasingly used in accordance with manufacturer IFUs. The higher number of studies reporting results in asymptomatic participants has contributed to small improvements in methodological standards in regard to the reference standard. However, some concerns about risk of bias and applicability of results remain, and further improvements in study methods and reporting could be implemented by study authors.

Particular methodological concerns that remain include the use of deliberate sampling according to known presence or absence of SARS-CoV-2 infection, a lack of information about the presence of symptoms or time from symptom onset and poor reporting about blinding of index and reference standard interpretation. Differences in case-mix related to symptomatic status, time post-symptom onset and distribution of viral load are likely to have contributed to the observed variation in accuracy. RT-PCR was the reference standard for the presence of infection in all studies apart from one using an alternative molecular method (TMA) - no study defined the presence of COVID-19 using clinical or radiological features in the absence of a negative RT-PCR result, and the majority continue to rely on a single negative RT-PCR as evidence of absence of infection.

3. Compliance with manufacturers' instructions was relatively poor

There has been an improvement in the reporting of tests being used at the point of care as opposed to in centralized laboratory settings, however studies frequently did not follow the manufacturer IFUs in regard to sample type, and timing of tests. Fewer than half conducted the tests according to the manufacturer IFU (43% (90/210) compared to 50% (29/58) of antigen test evaluations in the previous review iteration). Non-compliance with IFUs was frequently because VTM was used when this was either not recommended by the manufacturer or the manufacturer did not provide instructions for use with VTM, or because lengthy intervals between sample collection and testing were reported (often with a period of frozen storage). Of the 113 (54%) evaluations reporting direct swab testing, 85 complied with manufacturer IFUs. Reasons for non-compliance were use of samples not specified on the IFU ($n = 17$), or samples were tested after the time limit specified on the IFU ($n = 10$), or the time delay between sample collection and testing was not specified ($n = 7$). Only 29% of antigen test evaluations included in the last iteration of this review in March 2021 reported on-site, direct swab testing immediately or within an hour of sample collection.

4. Small number of assays meet minimum acceptable sensitivity requirements in symptomatic participants

For antigen test evaluations in symptomatic participants, we observed a similar pattern of results as for the previous review iteration. Considerable heterogeneity in sensitivities (and to a lesser extent the specificities) remained, however the increase in number of evaluations and samples analysed increased confidence in the observed results. The average sensitivity of RDTs in symptomatic populations was 73.0% (95% CI 69.3% to 76.4%) and specificity 99.1% (95% CI 99.0% to 99.2%). Average sensitivity decreased with time since onset of symptoms, being higher in the first week (80.9%, 95% CI 76.9% to 84.4%) than when done in week two or later (48.9%, 95% CI 37.9% to 60.1%), but with similarly high specificities at both time points (99.2% and 99.5% on

average). We were also able to demonstrate higher sensitivities for individuals presenting to COVID-19 testing centres compared to all other settings.

Focusing on studies that used the test in accordance with the manufacturer's instructions, sensitivities for different brands varied from 34% to 91% in symptomatic participants (either based on summary results or single studies). The WHO has set a minimum 'acceptable' sensitivity requirement of 80%, ($\geq 90\%$ 'desirable') and acceptable and ideal (or 'desirable') specificity requirements of 97% and 99% respectively (WHO 2020b). Seven assays (from AAZ, Abbott (BinaxNOW), BIONOTE, Denka Co, LumiraDx, Quidel, and Shenzhen Bioeasy) met the WHO acceptable criterion for sensitivity based on summary results of several studies, but the 95% confidence intervals for all results apart from for BIONOTE NowCheck overlapped the 80% standard. Two additional assays (from Mologic and from Siemens) also met the acceptable sensitivity criterion, but each test was evaluated in only one study. The 95% confidence intervals of the summary results for a number of other assays including Abbott Panbio overlapped the sensitivity criterion, but the point estimates were below 80%. The acceptable performance criterion of 97% specificity was also met for all tests apart from the Shenzhen Bioeasy assay.

Considerable heterogeneity in sensitivities remained after restricting analyses by test brand in symptomatic populations, suggesting an effect not only from participant characteristics but from setting, sample type and collection method, sample storage and preparation, and testing procedures that cannot be easily unpicked. For example, results by sample site suggest superior sensitivity from studies using nasal samples (76.6%, 95% CI 70.3% to 81.9%) compared to nasopharyngeal samples, either as the sole sample site, or in combination with oropharyngeal sampling in some or all participants (69.0%, 95% CI 65.3% to 72.4%). However, this suggestion of difference was not supported when the comparison was restricted to within-study comparisons of the two sampling sites. Limited data suggest lower RDT sensitivity for saliva and for oropharyngeal samples alone. Our previous review iteration pointed to possible differences in sensitivity according to test operator demonstrated in UK government-funded PHE studies of the Innova assay. Because of the various possible sources of confounding we did not carry out subgroup analyses by test operator for this version of the review. A single study directly comparing assay interpretation by test operator showed identical specificities and slightly higher sensitivity (by 2.5 percentage points) for the professional-interpreted tests compared to participant-interpreted tests. We are aware of additional studies examining the effect of self-collection and test operator on accuracy (e.g. Klein 2021), that will be considered for inclusion in the next review iteration.

5. Sensitivity is lower in asymptomatic participants but is higher if there is epidemiological exposure to SARS-CoV-2

Fifty studies reported data about the accuracy of antigen tests in asymptomatic people for detection of SARS-CoV-2 infection defined by PCR status (an increase from 13 in the previous iteration), including 17 conducted exclusively in asymptomatic or mainly asymptomatic populations. As discussed, this does not address the issue of whether the test is identifying those who are infectious (as there is no reference standard that can be used). The average sensitivity for detecting infection in asymptomatic participants was 54.7% (95% CI 47.7% to 61.6%) with specificity of

99.5% (95% CI 99.4% to 99.6%), 18.2 percentage points lower than for symptomatic populations (95% CI from -26.1 to -10.4 percentage points). Unlike for the previous review iteration however, for this review we were able to conduct some subgroup analyses by eligibility for testing and setting. Considerably higher summary sensitivities were observed when an epidemiological exposure to SARS-CoV-2 was suspected (sensitivity 64.3%, 95% CI 54.6% to 73.0%) or for asymptomatic participants presenting to COVID-19 test centres (61.5%, 95% CI 54.0% to 68.4%), compared to studies where RDTs were reportedly widely available to anyone presenting for testing (sensitivity 49.6%, 95% CI 42.1% to 57.1%) or for evaluations considered to represent screening scenarios (45.1%, 95% CI 36.4% to 54.1%) or school or university-wide testing programmes (47.9%, 95% CI 38.1% to 57.9%).

Three evaluations reporting data by time after exposure to infection in asymptomatic participants provided weak evidence for higher RDT sensitivity in week 1 (70.0%, 95% CI 60.8% to 77.8%) compared to week 2 (60.7%, 95% CI 48.0% to 72.0%) after exposure.

There was considerable variation in sensitivities in asymptomatic participants between test brands, however the number of evaluations per test brand was small such that for many brands heterogeneity is likely to be strongly influenced by setting, timing and indication for testing of asymptomatic people.

6. Steady decline in sensitivity with lower viral load

For this version of the review, sufficient data were available for a more detailed investigation of RDT accuracy by viral load, moving away from an overly simplistic dichotomous analysis of results above and below any single Ct or RNA copies/mL threshold. A steady decline in RDT summary sensitivities was observed, from 97.4% (95% CI 95.0% to 98.6%) and 98.4% (95% CI 97.0% to 99.1%) in participant samples with the highest viral load (< 20 Ct or $\geq 10^7$ RNA copies/mL) to 68.7% (95% CI 61.6% to 75.0%) and 70.9% (95% CI 57.4% to 81.5%) for samples in the 25 to 30 Ct or 10^5 RNA copies/mL range. Considerably lower average sensitivities were observed in the lowest viral load subgroups, for example, 7.5% (95% CI 3.8% to 14.3%) for those with < 10^4 RNA copies/mL and 36.7% (95% CI 24.7% to 50.5%) for samples with 10^4 RNA copies/mL. Data according to 'viral load' was contributed from studies including both symptomatic and asymptomatic participants. We were not able to consider any effect from symptom status on viral load patterns because of relatively low numbers of evaluations.

At lower Ct values and higher RNA copies/mL, different test brands appear to perform relatively consistently, with a few exceptions. As Ct increases and RNA copies/mL falls, we observed considerably greater heterogeneity in sensitivity, however it is not clear whether there are systematic differences in assay performance for samples with lower viral loads or whether other differences between studies might explain the observed variability. Studies comparing analytical sensitivities between brands however, suggest true differences in the ability of different assays to detect lower concentrations of virus (e.g. [Karon 2021](#); [Mak 2021](#)). What is not clear is the extent to which missed cases with samples in the mid to low range of viral load could be contributing onward transmission of infection.

7. Suggestion of lower sensitivity in children

Limited data suggest possibly lower sensitivity but similar specificity in children. Using all data reported for children, average

sensitivity was 62.7% (95% CI 52.7% to 71.7%) and average specificity 99.4% (95% CI 99.1% to 99.6%). Restricting the analysis to studies reporting data for both children and adults (thereby minimising other differences between groups) average sensitivity was 9.9 percentage points higher (95% CI -8.7 to 28.4; a difference that might be observed by chance), and average specificity 0.7 percentage points higher (95% CI 0.2 to 1.2) in adults compared to in children. With increasing evidence that viral loads are similar between children and adults ([Chung 2021](#); [Madera 2021](#); [Yonker 2021](#)), other factors such as the adequacy of sampling, timing of testing in relation to onset of infection, or participant characteristics, are likely to have contributed to the observed results.

8. Limited evidence for repeat testing strategies

Repeated use of antigen tests in different asymptomatic groups, such as school children and staff, hospital and care home workers, and the general public is increasingly advocated. We found only four eligible studies evaluating the accuracy of repeated testing within our search period. The studies varied in purpose, design, testing strategies and presentation of results such that it is not possible to make generalizations about the value of repeated testing strategies. Setting aside the study with only one PCR-positive case ([Kriemler 2021](#)), one study suggested that regular weekly testing of asymptomatic adults might pick up around 90% of those with pre-symptomatic or early infection ([Winkel 2020](#)), however the number of cases detected was relatively small and confidence intervals wide. Specificities were close to or above 99% in both studies of weekly testing.

A feasibility study of daily contact testing suggested this approach could detect between 68% of asymptomatic and 89% of symptomatic cases ([Love 2021](#)); PCR Ct values of cases missed by the RDT ranged from 16.9 to 32.1 however this may not fully reflect Ct values at the time of the RDT because of delays between RDT and PCR sample collection. The final study reported results of repeated daily testing in those with at least one sample with successful viral culture ([Smith 2021](#)); in the days prior to successful viral culture the RDT used was considerably less sensitive than either direct saliva RT-PCR or conventional nasal swab RT-PCR and only demonstrated similar sensitivity (within 10 percentage points of conventional RT-PCR) for samples obtained on the day that viral culture became positive up to day 2 after viral culture positivity. Model-based estimates of the sensitivity of different testing strategies suggested that daily RDTs would be needed to detect 90% of PCR-positive cases, dropping to only 80% sensitivity for testing every three days ([Smith 2021](#)).

Additional studies of repeated testing that did not report results as accuracy estimates suggest sub-optimal detection rates from RDTs compared to PCR in the days leading up to onset of symptoms ([Basile 2021](#)), and further, that even daily RDT testing may not be sufficient to contain transmission ([Moreno 2021](#)).

We have already identified a number of additional studies of repeated testing strategies for consideration for the next update of this review (e.g. [Aranda-Diaz 2021](#); [Harmon 2021](#); [Kanji 2021](#); [Kweon 2021](#); [McKay 2021](#); [Shah 2021](#); [Sterbenc 2021](#); [Young 2021a](#)). Studies listed in [Characteristics of studies awaiting classification](#) are those already identified as eligible (according to current review eligibility criteria) up to August 2021 with additional searches completed up to October 2021.

Illustration of predicted effect of antigen testing by symptom status

Below we illustrate predicted numbers of true positives, false positives, false negatives and true negatives, applying summary estimates of test accuracy to hypothetical cohorts of symptomatic or asymptomatic people suspected of SARS-CoV-2 infection across a range in prevalence of SARS-CoV-2 infection ([Summary of findings 1](#)).

For antigen test evaluations in symptomatic people, we used data for all symptomatic participants combined (sensitivity 73.0%, 95% CI 69.3% to 76.4%, and specificity 99.1%, 95% CI 99.0% to 99.2%), and data for symptomatic participants tested during the first week after symptom onset (sensitivity 80.9%, 95% CI 76.9 to 84.4% and specificity 99.5%, 95% CI 99.3% to 99.6%). The latter estimates are also in the range of those observed for symptomatic people presenting for testing at COVID-19 test centres. Applied to a cohort of 1000 people with signs and symptoms of COVID-19, in whom 50 people had confirmed infection (prevalence of 5%), we predicted that:

- 46 (overall) or 45 (week 1) people would have a positive test result, of which 9 or 5 would be false positives (positive predictive values (PPV) 81% and 89%, respectively), and
- 14 (overall) and 10 (week 1) people with negative test results would be falsely negative (negative predictive values (NPV) 98.6% and 99.0%).

Increasing the prevalence to 10% or 20%, increases PPV to 90% or more and slightly decreases NPV. As there is some heterogeneity in the estimates of sensitivity, the values observed in practice could vary slightly from these figures as shown by the estimates derived from the confidence intervals for the summary estimates ([Summary of findings 1](#)).

For antigen test evaluations in asymptomatic participants we used subgroup data according to whether testing was reported to be widely available to any asymptomatic person with no requirement to meet pre-set criteria for testing (sensitivity 49.6%, 95% CI 42.1% to 57.1%, and specificity 99.6%, 95% CI 99.5% to 99.7%) and where testing was restricted to those reporting epidemiological exposure to COVID-19 (sensitivity 64.3%, 95% CI 54.6% to 73.0%, and specificity 99.7%, 95% CI 99.5% to 99.8%). Applying the average values to a larger cohort of 10,000 people asymptomatic for COVID-19 and with a lower prevalence of 0.5% in whom 50 people had confirmed infection (infectious or not):

- 65 (widely available) or 62 (epidemiological exposure) individuals would have a positive test result of which 40 and 30 would be false positives (PPVs of 38% and 52%, respectively), and
- 25 (widely available) and 18 (epidemiological exposure) people with negative test results would be falsely negative (NPVs 99.7% and 99.8%).

The confidence intervals for the average sensitivity estimates used in these calculations are relatively wide, such that the number of false negatives observed in practice could differ from these figures, as can be seen from the estimates derived from the confidence intervals. However, at very low prevalence of disease, as might be seen in a mass screening scenario, the effect on the absolute number of false negatives observed could be small (e.g. from

21 to 29 using the 95% CIs for the average sensitivity where testing was widely available). In contrast, although the 95% CIs for average specificities were only 0.2 to 0.3 percentage points wide the absolute numbers of false positives ranged between 20 and 50.

Increasing the prevalence of confirmed SARS-CoV-2 infection to 1% or 2% makes little difference to the absolute number of false positive results, but has a large relative effect when considered in relation to the total number of positive test results (true and false positives; PPVs increasing to 72% for widely available testing and 81% for testing contacts of confirmed cases at 2% prevalence; [Summary of findings 1](#)).

Strengths and weaknesses of the review

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 assessments ([Whiting 2011](#)), 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. Whilst we have reasonable confidence in the completeness and accuracy of the findings up until the search date, should errors be noted please inform us at covidtda@contacts.bham.ac.uk so that we can verify and correct in our next update. The review is however limited by the March 2021 cut-off for the electronic searches. While the effect of this is mitigated to some extent by including studies from other sources up to 30 April 2021, we are aware of a large number of eligible studies published or available as preprints in the interim period. Full-text assessment of studies available up to 18 August 2021 has resulted in 84 studies that will be eligible for a subsequent review update according to current review inclusion criteria (described in [Characteristics of studies awaiting classification](#)). A brief review of these studies indicates that their inclusion in the review will further strengthen rather than change our conclusions about the accuracy of single applications of a test for diagnostic or screening purposes, however we anticipate inclusion of additional information about the accuracy of repeated testing strategies.

We explicitly considered whether the test evaluations were conducted in accordance with the manufacturer IFU, regarding the sample types used, the use of VTM and the permitted time between sample collection and testing. We did not however consider any manufacturer statements on the intended use of the tests by population, but we are aware that some IFUs recommend testing only in symptomatic people and within certain time frames after symptom onset (see Appendix 9). Instead, we have provided data separately for symptomatic and asymptomatic participants and identified clear evidence of lower sensitivities in asymptomatic individuals for detection of infection.

We did not attempt to assess the accuracy of antigen tests for identification of infectious individuals, as there is no established reference standard for infectiousness (and it seems unlikely that one will ever be established). For the first time, however, data have permitted presentation of results according to 'viral load' in smaller subgroups by Ct value or by RNA copies/mL, the latter approach going at least some way to addressing variation in RT-PCR Ct values between assays ([Vogels 2020](#)), and between laboratories. Our results support a steady deterioration in summary sensitivity as

viral load (or at least these proxy measures of viral load) decreases, and relatively poor assay sensitivity (around 70%) for samples with mid-range Ct or RNA copies/mL values. As previously discussed, there is no 'step change' in 'infectiousness' according to any fixed Ct value; increasing numbers of studies demonstrate successful viral culture in individuals considered to have 'low' viral load (Jaafar 2020; Singanayagam 2020), and, more importantly, that transmission of infection does occur from index cases with high RT-PCR Ct values (Lee 2021; Marks 2021; Tian 2021). A large Danish study looking at household transmission found that 34% of all secondary cases (almost 30,000 total cases) were in households where the primary index case had Ct values of 30 or more (Lyngse 2021). Ultimately, viral load on its own is only one factor influencing an individual's ability to transmit infection, 'infectiousness' being modified by host factors such as the health of an individual's immune system, vaccination status, presence of comorbidities, and environmental risk factors including closeness and length of contact with others.

Thus far we have also been unable to systematically consider test accuracy for detection of more infectious SARS-CoV-2 variants of concern such as Delta and, more recently Omicron (B.1.1.529), or to consider whether test accuracy might vary between vaccinated and unvaccinated individuals. Studies of analytical accuracy for detection of different variants (including Alpha and Delta variants) have suggested no consistent effect on test accuracy, with most RDTs examined to date showing similar accuracy regardless of variant (Bekliz 2021; Frediani 2021; Lindner 2021). It is too early to determine whether variations in accuracy might be observed for detection of the Omicron variant in clinical performance evaluations. Thus far, a small UK Health Security Agency laboratory-based evaluation found no evidence for impaired analytical sensitivity of five different RDTs (UK HSA 2021b), however the Food and Drug Administration (FDA) have released a statement advising potentially reduced sensitivity of RDTs for detection of the Omicron variant (FDA 2021).

Weaknesses of the review primarily reflect the weaknesses in the primary studies and their reporting. Although small improvements in study quality were observed, a good proportion of studies continue to omit descriptions of participants, and key aspects of study design and execution. In order to include data for all tests in meta-analyses we had to include some samples multiple times. We have been explicit about these issues where they arose. It is possible that eligible studies have been missed by our search strategy however we believe the risk to be very low considering our broad approach to identification of literature. Despite our best efforts to be as comprehensive as possible, new evaluations are continuously becoming available and it is impossible for any published and peer-reviewed systematic review to be fully up to date.

We are aware of one other systematic review of antigen detection tests that covers a similar search period to our review, with electronic searches to 30 April 2021 (Brümmer 2021). There is a very high degree of overlap in included studies between the two reviews and a similar approach to overall analysis of studies was taken. Our review however includes a much higher number of samples from asymptomatic participants (e.g. 40,956 samples from 50 evaluations compared to 15,228 samples from 25 evaluations in Brümmer 2021), allowing us to conduct a more detailed analysis by study setting and indication for testing. We have also taken a

different approach to analyses by viral load (data categorized in smaller subgroups as opposed to analyses above and below single threshold values).

Around a fifth (25/130) of primary study reports are only available as preprints, and as yet, have not undergone peer review (a fall from 25% of primary study reports in the previous review iteration). As published versions of these studies are identified in the future, we will double-check study descriptions, methods and findings, and update the review as required.

Applicability of findings to the review question

There are an increasing number of roles and testing strategies for which rapid antigen assays are considered, and it is likely that the performance of these tests needs to be considered separately for each of the use cases. It is notable that the majority of studies were conducted in Europe or North America (116/152) and it is not fully clear whether results will generalize to low- or middle-income countries

Our review shows that on average antigen tests do not perform as well in asymptomatic populations compared to symptomatic populations for detecting infection. However, asymptomatic individuals may be tested in a range of scenarios, from preventive or targeted screening, to contact tracing or testing at dedicated COVID-19 test centres. We have been able to demonstrate higher RDT sensitivity when used in individuals likely to have had a recent epidemiological exposure to a confirmed case, or in asymptomatic individuals presenting for testing at a COVID-19 test centre, or both, compared to assay use in 'mass' screening scenarios where asymptomatic individuals are encouraged to present for testing regardless of epidemiological indications. Lower sensitivities in the latter group will be affected by a number of factors, including time since exposure to infection and a potentially shorter timeframe in which asymptomatic people have higher viral loads. Variation in viral trajectories between individuals (Cevik 2021), also mean that even when an asymptomatic person can identify a clear contact with a confirmed case of SARS-CoV-2 infection, it is not possible to pinpoint when (or even if) that individual will have a sufficient viral load to be detected on antigen testing.

Incomplete symptom assessment and lack of adequate follow-up to identify subsequent development of symptoms or previous history of symptoms can all contribute to inappropriate classification of individuals as having asymptomatic infection (Meyerowitz 2020). Although we have been able to consider the effect of study setting and indication for testing in more detail than previously, the estimates for test accuracy for asymptomatic populations primarily represent accuracy in those without clearly defined symptoms at the time of testing. Two studies of repeated antigen testing in asymptomatic people did however suggest higher RDT sensitivities for those who went on to develop symptoms or for those who were tested early during the course of infection. Serial testing may only achieve optimal levels of sensitivity (90% or more) when implemented on a daily basis however, and furthermore this does not mean that all potentially infectious cases of SARS-CoV-2 would be picked up. We are aware that several studies of asymptomatic testing have been reported since the close of our search and will further contribute to the debate around optimal targeted deployment of antigen detection tests in asymptomatic individuals (Caruana 2021; Fernandez-

Montero 2021; Kumar 2021a; Norizuki 2021; Revollo 2021; Sood 2021; Sterbenc 2021).

AUTHORS' CONCLUSIONS

Implications for practice

We consider the implications for practice for this review separately for symptomatic and for asymptomatic testing.

In the [Role of index test\(s\)](#) section, we suggested that for symptomatic individuals, and if sufficiently accurate, point-of-care testing could be used either to replace laboratory-based reverse transcription polymerase chain reaction (RT-PCR) or as a triage to RT-PCR. As point-of-care tests are more accessible and provide a result more quickly than RT-PCR, theoretically their use may increase detection and speed up isolation and contact-tracing, leading to reduction in disease spread and reduce the burden on laboratory services.

The evidence included to date suggests the following.

1. For diagnosis in symptomatic individuals in the first few days of symptoms, the most accurate rapid antigen tests are a useful alternative to laboratory-based RT-PCR where immediate results are required for timely patient management or where there are significant logistical or financial challenges in delivering RT-PCR in a timely manner. Rapid antigen tests are only sufficiently sensitive in the first week after onset of symptoms. This conclusion can be considerably strengthened in comparison to the previous iteration of this review.

We have continued to observe variable sensitivity between assay brands. Only those shown to meet appropriate criteria, such as the World Health Organization's (WHO) priority target product profiles for COVID-19 diagnostics (i.e. sensitivity $\geq 80\%$ and specificity $\geq 97\%$; [WHO 2020b](#)), could be considered as a rational substitute for RT-PCR.

Tests had high specificity, thus in symptomatic populations (where prevalence is likely to be high) the risk of false positives is low. At 80% sensitivity compared to RT-PCR, the probability that infected individuals are missed is 20% higher than for RT-PCR. Thus the possibility of false negative results should be considered in those with a high clinical suspicion of COVID-19, particularly if tested several days after onset of symptoms when viral load levels may have fallen.

2. Rapid antigen tests could be used simultaneously with RT-PCR for symptomatic people, particularly where RT-PCR turnaround times are slow, to exploit the benefits of earlier results and consequent contact-tracing and isolation. Given the risk of false-negative results, isolation may be required until RT-PCR-negative results are obtained. Similarly, for investigation of local outbreaks, rapid antigen testing in a clearly defined population may establish cases and contacts that require isolation whilst awaiting results from RT-PCR.

In other circumstances rapid antigen tests may be used to triage to follow-on RT-PCR tests (rather than all receiving PCR tests) dependent on prevalence and the consideration of the consequences of false positive and false negative results.

Where prevalence is low, positive rapid test results in symptomatic individuals require confirmatory testing to avoid unnecessary quarantine measures (positive predictive values (PPVs) around 80% to 90% for antigen assays mean that between 1 in 5 and 1 in 10 positive results will be falsely positive). Self-isolation for the duration of symptoms in those with negative rapid test results should minimize the effect on transmission of infection from missed cases. Where available, testing by RT-PCR may be reasonable for people with a high clinical suspicion of COVID-19 and negative rapid test.

Where prevalence is higher (i.e. 20% or higher), false positives are less of a concern (PPVs around 95%) but the impact from false negative results becomes increasingly important and all test negatives may be considered for verification. At 20% prevalence, and using data for symptomatic people presenting to COVID-19 test centres, around 4% of those with negative rapid test results are missed cases of SARS-CoV-2 (30 to 40 cases missed out of a total of 200 cases). The lower the negative predictive value (NPV), the greater the potential effect on transmission of infection from missed cases and greater the impact from delays in commencement of contact tracing. For scenarios in which positive results do not have confirmatory testing, it is important that assays with high specificities (in the range of 99% to 100%) are selected in order to minimize the impact from false positive results at higher prevalences of disease.

3. We found some evidence for higher sensitivity in people with a known exposure to SARS-CoV-2 compared to testing scenarios more to akin mass screening of asymptomatic individuals

The key focus in mass screening is identification of individuals who are or will become infectious. PCR-positives define those who had detectable viral particles on their swab, which will include most of those who are or will become infectious, but also include individuals post-infection with residual viral particles. Without a reference standard for infectiousness, test accuracy studies cannot assess the ability of the test to detect the infectious subgroup of infections, and cannot provide evidence as to how well rapid antigen tests differentiate between individuals requiring isolation and those who provide no risk. The effectiveness of mass screening using these tests will ultimately only be established through participant outcome studies, such as cluster-randomized community trials.

Rapid tests demonstrating the highest specificities (i.e. 99% and above) should be considered for use during a period of outbreak or in those with likely exposure to SARS-CoV-2, as those found testing positive will have a high chance of being true positives, and thus the test can be used to identify cases requiring isolation. Consideration should be made as to whether test positives should be confirmed with PCR to identify false positives. With a 1% prevalence, and using average sensitivity and specificity for those likely to be contacts of confirmed cases, as much as a third (32%) of those with positive results would be falsely positive. Using data more likely to represent mass screening scenarios, at 1% prevalence, on average RDTs yield as many false positives as true positives (PPV 52%), and at 0.5% prevalence, false positives more than outweigh true positives (PPV 38%) even for tests with 99% specificity ([Summary of findings 1](#)).

However, the low and variable sensitivity, and lack of evidence that those who test negative are not, or will not become, infectious indicates that those who are rapid antigen test-negative cannot be

considered free of risk of being, or of becoming, infectious. In any screening or mass testing programme people testing negative still have a risk of infection.

4. Evidence about test accuracy in at-risk asymptomatic groups, such as hospital workers, or during local outbreaks at schools, workplaces, or care homes remains relatively limited. Although we might expect tests to perform similarly to testing of contacts the potential impact of low-sensitivity tests in these settings is greater than for mass screening or testing at COVID-19 test centres; false negatives in at-risk groups have greater potential to either create new outbreaks or to increase the severity of existing outbreaks. Further research in these settings is still needed.

5. We were only able to include limited evidence on the repeated use of tests. Studies of daily testing suggested lower sensitivities in those who remained asymptomatic during the testing period and optimal levels of sensitivity for the RDT only on the immediate days after successful viral culture. Although serial testing (over a number of days), or combinations of different rapid tests (e.g. an antigen test followed by a rapid molecular test) on the same sample are proposed to overcome the limitations of on average low test sensitivity, they all require further validation, both in symptomatic (e.g. as a green flag for release from self-isolation) and asymptomatic (e.g. to avoid quarantine in contacts of confirmed cases) populations. Use of multiple tests may increase false positive results, and there are likely to be many individuals with repeated false negative results reducing the expected benefit of subsequent tests. It is unlikely that models will be able to predict how well repeated tests and test combinations would work.

Overall, our conclusions have considerably strengthened those from the first version of this review and allowed some consideration of test accuracy in different testing scenarios. Ultimately, decisions around rapid testing will be driven not only by diagnostic accuracy but by acceptable levels of test complexity, time to result, access and acceptability to those being tested, and how test results influence individual behaviour, all of which might vary according to the setting in which the tests are to be used.

Implications for research

There is now a considerable volume of research for point-of-care tests for SARS-CoV-2 infection, particularly in symptomatic populations. Nevertheless, evidence for the clinical performance of many test brands is scarce or lacking, and well designed prospective and comparative evaluations of different test brands in clinically relevant settings (both for symptomatic and asymptomatic testing) are still needed. Studies should recruit consecutive series of eligible participants and should clearly describe the clinical status, document time from symptom onset or time since exposure. Point-of-care tests must be conducted in accordance with manufacturer instructions for use, and across the spectrum of point-of care settings and test operators. Evaluations of both individual tests and strategies of repeated testing are needed.

Consideration needs to be made of the best method for evaluating screening programmes, whether mass screening or targeted approaches including schools, healthcare setting and traveller screening. Whilst test accuracy studies help indicate which tests are likely to detect the greatest numbers of cases with the fewest false positives, assessing whether detecting asymptomatic cases leads

to worthwhile reductions in disease spread will only be properly answered by studies of impact not accuracy.

Manufacturers and independent investigators are strongly encouraged to consider the principles for test evaluation set out by the Royal Statistical Society Diagnostic Tests Working Group (RSS 2021).

Any future research study needs to be clear about eligibility and exclusion decisions throughout the whole diagnostic pathway, and should conform to the updated Standards for Reporting of Diagnostic Accuracy (STARD) guideline (Bossuyt 2015).

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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]

Abdelrazik 2021
Study characteristics

Patient Sampling	<p>Multi-group study to estimate sensitivity and specificity including: [1] symptomatic PCR+ve patients (n = 160) [2] exposed HCWs and patient contacts (n = 150) Data are presented only for groups [1] and [2] combined; author contacted 15 March 21</p> <p>Recruitment: unclear (do not state all patients)</p> <p>Prospective or retrospective: not stated; appears prospective</p> <p>Sample size (cases): 310 (188)</p>
Patient characteristics and setting	<p>Setting: mixed; described as patients, their contacts and exposed HCWs</p> <p>Location: Fayoum University Hospital, Fayoum</p> <p>Country: Egypt</p> <p>Dates: May 2020</p> <p>Symptoms and severity: unclear; 160 PCR+ve "patients" presumably symptomatic, plus 150 presumably asymptomatic contacts and exposed HCWs</p> <p>Demographics: median age 42 years; 184/310 (59%) male</p> <p>Exposure history: states "exposed healthcare workers and patient contacts."; no further details</p>
Index tests	<p>Test name: BIOCREDIT COVID-19 Ag kit</p> <p>Manufacturer: not stated; manufacturer is RapiGEN</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Abdelrazik 2021 (Continued)

	Antibody: not stated Ag target: not stated Test method: CGIA; described as lateral flow immunochromatographic assay (uses a dual-colour system for the qualitative detection of the SARS-CoV-2 antigen) Samples used: NP using flocked swabs; collection not specified Transport media: UTM-RT System, Copan Diagnostics, Murrieta, CA Sample storage: transported to lab within 1-2 h of collection; stored at 4 °C and tested within 24 h Test operator: laboratory staff Definition of test positivity: no details Blinding reported: unclear; index test performed after PCR test Timing of samples: group [1] (n = 160) median 3 days pso
Target condition and reference standard(s)	Reference standard: PCR (multiplex real-time PCR detection kit; DTlite 4, Russia) Definition of non-COVID cases: as for cases; single negative Genetic target(s): not stated Samples used: NP in VTM; same as for index test Timing of reference standard: as for index test Blinded to index test: yes (PCR performed before index test) Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; same swab All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
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		

Abdelrazik 2021 (Continued)

Was a case-control design avoided?	No	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	
If a threshold was used, was it pre-specified?	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?		High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Abdelrazik 2021 (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Abdulrahman 2020
Study characteristics

Patient Sampling

Single-group study to estimate sensitivity and specificity: mildly symptomatic individuals with suspected COVID-19 cases (defined by Bahrain protocol), referred to the national testing centre

Recruitment: not stated; appears consecutive

Prospective or retrospective: prospective

Sample size (cases): 4183 (733)

Patient characteristics and setting

Setting: national COVID-19 test centre

Location: symptomatic hall in the National Testing Centre at the exhibition centre

Country: Bahrain

Dates: not stated

Symptoms and severity: all mild symptomatic individuals
 Median symptom duration: 2 (range 0-14) days; only collected for 1301 (31%)

Demographics: mean age 30.9 ± 14.5 years; 2365 (56.5%) male

Exposure history: not stated

Index tests

Test name: Panbio COVID 19 antigen rapid test

Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany

Antibody: SARS-CoV-2 nucleocapsid protein

Ag target: not stated

Test method: CGIA

Samples used: nasal (NMT); trained HCW collected the samples using NP swab based on CDC guidelines (patient's head tilted back by 70°, swab inserted 2 cm into the nostril, gently rotated, rolled several times and removed)

Transport media: none; immediate on-site testing

Sample storage: none

Test operator: not stated; most likely trained HCW as the test was conducted on site

Definition of test positivity: not stated

Blinding reported: yes; test was conducted on site before PCR test

Timing of samples: 1301 (31%) = median of 2 (range 0-14) days pso

Abdulrahman 2020 (Continued)

Target condition and reference standard(s)	<p>Reference standard: RT-PCR, in-house assay following WHO protocol; Ct values > 40 on E gene were considered negative (used Thermo Fisher Scientific TaqPath 1-Step RT-qPCR Master Mix)</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): E gene confirmed by RdRP and N genes</p> <p>Samples used: NP swab in VTM</p> <p>Timing of reference standard: 1301 (31%) = median of 2 (range 0-14) days pso</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous; paired swab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none; states "no equivocal results were reported for index or reference"</p> <p>Uninterpretable results: none</p> <p>Indeterminate results (index test): none</p> <p>Indeterminate results (reference standard): none</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: none received</p> <p>Publication status: preprint</p> <p>Source: medRxiv</p> <p>Author COI: authors report no COI present</p>

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 inclusions?	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

Abdulrahman 2020 (Continued)

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Agullo 2021 [A]
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Agullo 2021 [A] (Continued)

Patient Sampling	<p>Single-group study (from 3 centres) to estimate sensitivity and specificity: consecutive adults and children, either with COVID-19 signs/symptoms or asymptomatic contacts</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 659 (265); 610/659 also provided saliva samples</p>
Patient characteristics and setting	<p>Setting: primary care</p> <p>Location: 3 primary care centres in Spain (organized by Hospital General Universitario de Elche)</p> <p>Country: Spain</p> <p>Dates: 15 September-29 October 2020</p> <p>Symptoms and severity: 265 (40.2%) patients were asymptomatic and 394 (59.8%) had symptoms, with median (IQR) duration of 3 (2-5) days</p> <p>Demographics: median (IQR) age: 38 (21-49.8) years; 76 (11.5%) ≤ 14 years, 45 (7.6%) > 65 years, 372 (56.4%) women</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Panbio COVID 19 antigen rapid test</p> <p>Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany</p> <p>Antibody: SARS-CoV-2 nucleocapsid protein</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] NP; [B] nasal (both collected by qualified nurse); [C] saliva (self-collected)</p> <p>Transport media: none; immediate on-site testing</p> <p>Sample storage: none</p> <p>Test operator: not stated; may have been by same qualified nurse</p> <p>Definition of test positivity: not stated</p> <p>Blinding reported: yes; test was conducted on site before PCR test</p> <p>Timing of samples: median (Q1-Q3) duration of 3 (2-5) days of symptoms</p>
Target condition and reference standard(s)	<p>Reference standard: rRT-PCR testing was performed according to the manufacturer's guidelines on Cobas z 480 Analyser (Roche, Basilea, Suiza)</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): not specified</p> <p>Samples used: NP swab in VTM</p> <p>Timing of reference standard: as for index test; median (Q1-Q3) duration of 3 (2-5) days of symptoms</p> <p>Blinded to index test: not stated</p>

Agullo 2021 [A] (Continued)

	Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swab All participants received same reference standard: yes Missing data: not stated Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "this work was supported by the RD16/0025/0038 project as a part of the Plan Nacional Research+Development+Innovation (R+D+I) and co-financed by Instituto de Salud Carlos III - Sub- dirección General de Evaluación y Fondo Europeo de Desarrollo Regional; Instituto de Salud Carlos III (Fondo de Investigaciones Sanitarias [grant number PI16/01740; PI18/01861; CM 19/00160, COV20-00005])." Publication status: published Source: Journal of Infection Author COI: 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Agullo 2021 [A] (Continued)

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 (Evaluations of serial (repeat) testing)	
DOMAIN 3: Reference Standard	
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Agullo 2021 [B]

Study characteristics	
Patient Sampling	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Index tests	Test name: Panbio COVID 19 antigen rapid test

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Agullo 2021 [B] *(Continued)*

Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany
 Antibody: SARS-CoV-2 nucleocapsid protein
 Ag target: not stated
 Test method: CGIA
 Samples used: [A] NP; **[B] nasal** (both collected by qualified nurse); [C] saliva (self-collected)
 Transport media: none; immediate on-site testing
 Sample storage: none
 Test operator: not stated; may have been by same qualified nurse
 Definition of test positivity: not stated
 Blinding reported: yes; test was conducted on site before PCR test
 Timing of samples: median (Q1-Q3) duration of 3 (2–5) days of symptoms

Target condition and reference standard(s)	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Comparative	
Notes	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS

Agullo 2021 [C]
Study characteristics

Patient Sampling	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Index tests	<p>Test name: Panbio COVID 19 antigen rapid test</p> <p>Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany</p> <p>Antibody: SARS-CoV-2 nucleocapsid protein</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] NP; [B] nasal; (both collected by qualified nurse); [C] saliva (self-collected)</p> <p>Transport media: none; immediate on-site testing</p> <p>Sample storage: none</p> <p>Test operator: not stated; may have been by same qualified nurse</p> <p>Definition of test positivity: not stated</p> <p>Blinding reported: yes; test was conducted on-site before PCR test</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Agullo 2021 [C] *(Continued)*

Timing of samples: median (Q1-Q3) duration of 3 (2–5) days of symptoms

Target condition and reference standard(s)	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS
Comparative	
Notes	Comparative study of 3 sample types; Agullo 2021 [A] reports full study characteristics and QUADAS

Akingba 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: symptomatic individuals seeking COVID-19 testing at mobile testing units during community testing campaigns</p> <p>Recruitment: not specifically stated but appears to be consecutive; discussion states "unselected symptomatic individuals requesting testing"</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 677 (146)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centres; mobile testing sites (n = 6)</p> <p>Location: 6 community testing sites in Nelson Mandela Bay municipality, Eastern Cape</p> <p>Country: South Africa</p> <p>Dates: 17-20 November 2020</p> <p>Symptoms and severity: all symptomatic seeking COVID-19 testing (ambulatory; specific symptoms not reported)</p> <p>Demographics: age range: 3-85 years Sex: 59% female</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: PanBio SARS-CoV-2 RTD</p> <p>Manufacturer: Abbott Rapid Diagnostics, USA</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP (collection not described)</p> <p>Transport media: not stated; test buffer appears to be used</p> <p>Sample storage: immediate testing</p> <p>Test operator: not stated</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Akingba 2021 (Continued)

	Definition of test positivity: not stated; set by manufacturer Blinding reported: yes (on site prior to PCR) Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR; Seegene nCoV assay (single target positive, Ct > 38) Definition of non-COVID cases: as for cases; single negative Genetic target(s): not stated; states "3 targets", mean Ct values used Samples used: same as for index test (same swab after Ag testing) Timing of reference standard: not stated; as for index test Blinded to index test: not stated Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous (same swab) All participants received same reference standard: yes Missing data: yes; 19 excluded (see below) Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): 19/677 (2.8%) had inconclusive results (single target positive, Ct > 38) Unit of analysis: participant
Comparative	
Notes	Funding: no funding was given for this study Publication status: preprint (not peer reviewed) Source: medRxiv Author COI: the authors report 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	

Akingba 2021 (Continued)

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Albert 2020
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: patients with clinical suspicion of COVID-19 (compatible signs or symptoms appearing within the prior week) attending 1 of 8 primary care centres (n = 412)</p> <p>Recruitment: not stated; likely consecutive</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: primary care</p> <p>Location: 8 primary care centres of the Health Department Clínico-Malvarrosa in Valencia</p> <p>Country: Spain</p> <p>Dates: 2 September-7 October 2020</p> <p>Symptoms and severity: all symptomatic (< 7 days pso)</p> <p>Demographics: median age, 31 years (range, 1-91); 42% male 327 adults; median, 36 years (17-91 years) 85 children; median, 11 years (1-16 years)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Panbio COVID-19 AG Rapid Test Device (no product code reported)</p> <p>Manufacturer: Abbott Diagnostic GmbH, Jena, Germany</p> <p>Antibody: nucleoprotein</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP; collected by trained nurses using flocked swabs</p> <p>Transport media: none for Ag testing</p> <p>Sample storage: none</p> <p>Test operator: not stated; immediate testing</p> <p>Definition of test positivity: visible line within 15 min; as per manufacturer</p> <p>Blinding reported: yes</p> <p>Timing of samples: day < 7 pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, Massachusetts, USA)</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): ORF1ab, N and S genes</p> <p>Samples used: NP in UTM</p> <p>Timing of reference standard: as for index; tested within 24 h</p> <p>Blinded to index test: not stated; presume yes</p>

Albert 2020 (Continued)

	Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired All participants received same reference standard: yes Missing data: none reported; no participant flow diagram reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: this work received no public or private funds. Abbott Diagnostics provided Panbio COVID-19 AG Rapid Test Device kits. Publication status: preprint Source: medRxiv Author COI: the authors declare 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			Unclear

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Albert 2020 (Continued)

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Alemany 2021
Study characteristics

Patient Sampling	Single-group study including participants from 3 settings: [1] symptomatic individuals with suspected COVID-19 seen in routine practice (n = 446) [2] contacts exposed to positive PCR confirmed COVID-19 cases (n = 473) [3] preventive screening of unexposed asymptomatic individuals in the general population (n = 487) Recruitment: retrospective (frozen swabs) Prospective or retrospective: not stated
Patient characteristics and setting	Setting: mixed/unclear (laboratory-based) Location: not reported; multiple author institutions reported Country: Spain Dates: not stated

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Alemany 2021 (Continued)

Symptoms and severity: not stated; 15/1406 (1.1%) reportedly hospitalized (all PCR+)
Viral load of cases: Ct < 20, 258 (18.3%); Ct 20-24, 305 (21.7%); Ct 25-29, 285 (30.3%); Ct > 30, 103 (7.3%)

Demographics: all samples: mean age 40.4 years (SD 24.5), 453 (32.2% male)

Exposure history: 473/1406 (33.6%) identified through contact tracing

Index tests

Test name: Panbio™ COVID-19 Ag Test (no product codes). Selected following validation exercise using 40 NP samples to compare PanBio with Coris Bioconcept COVID-19 Ag RespiStrip, SD Biosensor STANDARD F COVID-19 Ag FIA and STANDARD Q COVID-19 Ag Test

Manufacturer: Abbott Laboratories, Illinois, USA

Antibody: not stated

Ag target: SARS-CoV-2

Test method: CGIA

Samples used: [1] and [2] NP, [3] NMT; collection not reported

Transport media: VTM (DeltaSwab Virus)

Sample storage: stored at 2-8 °C prior to PCR then frozen (-80 °C) prior to Ag testing; "Internal validation showed no significant change in the test performance using Abbot test Kit buffer or a mix of the Kit buffer and transport media at 1:3 dilution; likewise, the use of frozen specimens showed no significant differences compared with fresh ones"

Test operator: 2 laboratory technicians

Definition of test positivity: visible line; as per manufacturer

Blinding reported: yes

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: RT-PCR; in-house following CDC protocol

Definition of non-COVID cases: as per cases; single negative PCR for absence of infection

Genetic target(s): not stated; as per CDC protocol

Samples used: NP or NMT; as per index test

Timing of reference standard: fresh samples stored at 2-8 °C for up to 72 h prior to RT-PCR

Blinded to index test: yes; conducted first

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous (same swab)

All participants received same reference standard: yes

Missing data: none reported; no participant flow diagram reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Alemany 2021 (Continued)

Comparative

Notes

Funding: "the test kits were purchased from Abbott Rapid Diagnostics Healthcare SL (Spain). The funders of the study had no role in the study conception, design, conduct, data analysis, or writing of the report."

Publication status: preprint

Source: medRxiv

Author COI: authors declare 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		

Alemaný 2021 (Continued)

Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Aoki 2021
Study characteristics

Patient Sampling	Unclear design: samples from COVID-19 hospitalized patients or from patients with COVID-19-like symptoms Recruitment: unclear Prospective or retrospective: unclear Sample size (cases): 129 (63)
Patient characteristics and setting	Setting: appears to be laboratory-based; includes use of remnant samples Location: Toho University School of Medicine, Tokyo Country: Japan Dates: not stated Symptoms and severity: not stated Demographics: not stated

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Aoki 2021 (Continued)

	Exposure history: not stated
Index tests	<p>Test name: Espline SARS-CoV-2</p> <p>Manufacturer: Fujirebio Inc., Japan</p> <p>Antibody: SARS-CoV-2 N antigen (NeAg)</p> <p>Ag target: monoclonal antibodies</p> <p>Test method: immunochromatography assay based on sandwich enzyme immunoassay (ALP-labelled)</p> <p>Samples used: NP swab; collection not described</p> <p>Transport media: samples were collected into Espline swab buffer (ETS - Espline treatment solution) (n = 96); remnant samples were stored in UVT (n = 33)</p> <p>Sample storage: not described for samples in ETS; remnant samples in UVT been stored at -80 °C after PCR testing</p> <p>Test operator: not stated</p> <p>Definition of test positivity: "positive when both the reference line and the judgment line can be visually confirmed"</p> <p>Blinding reported: not stated</p> <p>Timing of samples: median 9.5 days pso for samples Ag+/PCR+, 16 days for Ag-/PCR+, 19 days for Ag-/PCR-</p>
Target condition and reference standard(s)	<p>Reference standard: PCR performed according to the "Pathogen Detection Manual 2019-nCoV Ver.2.6.1" from the National Institute of Infectious Diseases; assays included QuantStudio® 5 (Applied Biosystems, USA) or BD MAX open system</p> <p>Definition of non-COVID cases: single negative PCR for absence of infection</p> <p>Genetic target(s): gene N</p> <p>Samples used: paired NP swabs (one for Ag and one for PCR)</p> <p>Timing of reference standard: same as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: not clearly stated but appears to be 'simultaneous'</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none mentioned</p> <p>Uninterpretable results: none mentioned</p> <p>Indeterminate results (index test): none mentioned</p> <p>Indeterminate results (reference standard): none mentioned</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	Funding: Japan Agency for Medical Research and Development

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Aoki 2021 (Continued)

Publication status: published paper

Source: Journal of Infection and Chemotherapy

Author COI: SY is an employee of Fujirebio, Inc. The other study authors have no conflict 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?	Unclear		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Aoki 2021 (Continued)

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Unclear risk

Baro 2021 [A]
Study characteristics

Patient Sampling

Unclear design estimating sensitivity and specificity: unexposed asymptomatic individuals living in areas at high risk of an outbreak who participated in routine mass testing as part of a regional surveillance program (n = 316)

Recruitment: not stated; recruitment continued until at least 73 PCR+ and 165 PCR- samples were obtained

Prospective or retrospective: unclear

Sample size (cases): 286 (101)

Patient characteristics and setting

Setting: community screening; public health surveillance

Location: Catalonia (North-East Spain; i.e. Metropolità Nord) with a catchment population of ~1,400,000 people

Country: Spain

Dates: December 2020-January 2021

Symptoms and severity: states "all unexposed asymptomatic"

Demographics: not stated

Exposure history: states "all unexposed"

Index tests

Test name: **[A] PanBio™ COVID-19 Ag Rapid test**
 [B] CLINITEST Rapid COVID-19 Antigen Test
 [C] SD Biosensor SARS-CoV-2 Rapid Antigen Test
 [D] Lepu SARS-CoV-2 Antigen Rapid Test
 [E] Surescreen COVID-19 Coronavirus Rapid Antigen Test Cassette

Manufacturer: [A] Abbott Rapid Diagnostics, Panbio Ltd, USA
 [B] Siemens Healthineers (Shanghai International Holding Corp), USA
 [C] Roche Diagnostics, SD Biosensor, Republic of Korea

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Baro 2021 [A] (Continued)

[D] Beijing Lepu Medical Technology Co., Ltd., China

[E] SureScreen Diagnostics Ltd, UK

Antibody: nucleocapsid protein

Ag target: not reported

Test method: [A] CGIA

[B] Immunochromatographic

[C] LFA (unclear)

[D] CGIA

[E] LFA (unclear)

Samples used: NP (collected by HCW)

Transport media: VTM (DeltaSwab Virus, Deltalab; or UTM Universal Transport Medium, Copan)

Sample storage: samples stored for up to 24 h (2-8 °C) prior to RT-PCR then stored up to 12 h more at 2-8 °C until Ag testing

Test operator: lab technician at The University Hospital Germans Trias i Pujol

Definition of test positivity: visual coloured band; the presence of any test line (T) indicates a positive result. Samples were applied directly to the test cassette and incubated for 15 min at room temperature before reading results with the naked eye, according to the manufacturer IFU

Blinding reported: unclear; presume only blinded to different Ags tests

"All Ag-RDT determinations were performed in parallel by two blinded technicians"

Timing of samples: N/A; all asymptomatic

Target condition and reference standard(s)

Reference standard: RT-PCR; Allplex 2019-nCoV assay (Seegene, South Korea) on the CFX96 (Bio-Rad, USA)

Threshold according to the manufacturer's IFU

Definition of non-COVID cases: single negative PCR

Genetic target(s): not stated

Samples used: NP in VTM; performed on fresh samples stored at 2-8 °C for up to 24 h

Timing of reference standard: same as for index test

Blinded to index test: yes (performed before Ag tests)

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab used

All participants received same reference standard: yes

Missing data: 30/316 excluded; reasons for exclusion documented
 25 with no documented Ct value excluded a priori

Uninterpretable results: 1/316 incomplete result

Indeterminate results (index test): 4/316- all of them in the Lepu assay

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Baro 2021 [A] (Continued)

Notes

Funding: "Blueberry diagnostics, Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, and YoMeCorono.org crowdfunding campaign"

Publication status: preprint

Source: medRxiv

Author COI: authors declare 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?	Yes		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowl-	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Baro 2021 [A] (Continued)

edge of the results of the index tests?

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Baro 2021 [B]
Study characteristics

 Patient Sampling Comparative study of 5 Ag tests; [Baro 2021 \[A\]](#) reports full study characteristics and QUADAS

 Patient characteristics and setting Comparative study of 5 Ag tests; [Baro 2021 \[A\]](#) reports full study characteristics and QUADAS

Index tests

Test name: [A] PanBioTM COVID-19 Ag Rapid test
[B] CLINITEST Rapid COVID-19 Antigen Test
 [C] SD Biosensor SARS-CoV-2 Rapid Antigen Test
 [D] Lepu SARS-CoV-2 Antigen Rapid Test
 [E] Surescreen COVID-19 Coronavirus Rapid Antigen Test Cassette

Manufacturer: [A] Abbott Rapid Diagnostics, Panbio Ltd, USA
 [B] Siemens Healthineers (Shanghai International Holding Corp), USA
 [C] Roche Diagnostics, SD Biosensor, Republic of Korea
 [D] Beijing Lepu Medical Technology Co., Ltd., China
 [E] SureScreen Diagnostics Ltd, UK

Antibody: nucleocapsid protein

Ag target: not reported

Baro 2021 [B] (Continued)

Test method: [A] CGIA
 [B] Immunochromatographic
 [C] LFA (unclear)
 [D] CGIA
 [E] LFA (unclear)

Samples used: NP (collected by HCW)

Transport media: VTM (DeltaSwab Virus, Deltalab; or UTM Universal Transport Medium, Copan)

Sample storage: samples stored for up to 24 h (2-8 °C) prior to RT-PCR then stored up to 12 h more at 2-8 °C until Ag testing

Test operator: lab technician at The University Hospital Germans Trias i Pujol

Definition of test positivity: visual coloured band; the presence of any test line (T) indicates a positive result. Samples were applied directly to the test cassette and incubated for 15 min at room temperature before reading results with the naked eye, according to the manufacturer IFU

Blinding reported: unclear; presume only blinded to different Ags tests
 "All Ag-RDT determinations were performed in parallel by two blinded technicians"

Timing of samples: N/A; all asymptomatic

Target condition and reference standard(s)	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
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Flow and timing	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
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Comparative

Notes	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
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Baro 2021 [C]

Study characteristics

Patient Sampling	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
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Patient characteristics and setting	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
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Index tests	<p>Test name: [A] PanBio™ COVID-19 Ag Rapid test [B] CLINITEST Rapid COVID-19 Antigen Test [C] SD Biosensor SARS-CoV-2 Rapid Antigen Test [D] Lepu SARS-CoV-2 Antigen Rapid Test [E] Surescreen COVID-19 Coronavirus Rapid Antigen Test Cassette</p> <p>Manufacturer: [A] Abbott Rapid Diagnostics, Panbio Ltd, USA [B] Siemens Healthineers (Shanghai International Holding Corp), USA [C] Roche Diagnostics, SD Biosensor, Republic of Korea [D] Beijing Lepu Medical Technology Co., Ltd., China [E] SureScreen Diagnostics Ltd, UK</p> <p>Antibody: nucleocapsid protein</p> <p>Ag target: not reported</p> <p>Test method: [A] CGIA</p>
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Baro 2021 [C] (Continued)

[B] Immunochromatographic

[C] LFA (unclear)

[D] CGIA

[E] LFA (unclear)

Samples used: NP (collected by HCW)

Transport media: VTM (DeltaSwab Virus, Deltalab; or UTM Universal Transport Medium, Copan)

Sample storage: samples stored for up to 24 h (2-8 °C) prior to RT-PCR then stored up to 12 h more at 2-8 °C until Ag testing

Test operator: lab technician at The University Hospital Germans Trias i Pujol

Definition of test positivity: visual coloured band; the presence of any test line (T) indicates a positive result. Samples were applied directly to the test cassette and incubated for 15 min at room temperature before reading results with the naked eye, according to the manufacturer IFU

Blinding reported: unclear; presume only blinded to different Ags tests

"All Ag-RDT determinations were performed in parallel by two blinded technicians"

Timing of samples: N/A; all asymptomatic

Target condition and reference standard(s)	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Comparative	
Notes	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS

Baro 2021 [D]
Study characteristics

Patient Sampling	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Index tests	<p>Test name: [A] PanBio™ COVID-19 Ag Rapid test [B] CLINITEST Rapid COVID-19 Antigen Test [C] SD Biosensor SARS-CoV-2 Rapid Antigen Test [D] Lepu SARS-CoV-2 Antigen Rapid Test [E] Surescreen COVID-19 Coronavirus Rapid Antigen Test Cassette</p> <p>Manufacturer: [A] Abbott Rapid Diagnostics, Panbio Ltd, USA [B] Siemens Healthineers (Shanghai International Holding Corp), USA [C] Roche Diagnostics, SD Biosensor, Republic of Korea [D] Beijing Lepu Medical Technology Co., Ltd., China [E] SureScreen Diagnostics Ltd, UK</p> <p>Antibody: nucleocapsid protein</p> <p>Ag target: not reported</p> <p>Test method: [A] CGIA [B] Immunochromatographic</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Baro 2021 [D] (Continued)

[C] LFA (unclear)

[D] CGIA

[E] LFA (unclear)

Samples used: NP (collected by HCW)

Transport media: VTM (DeltaSwab Virus, Deltalab; or UTM Universal Transport Medium, Copan)

Sample storage: samples stored for up to 24 h (2-8 °C) prior to RT-PCR then stored up to 12 h more at 2-8 °C until Ag testing

Test operator: lab technician at The University Hospital Germans Trias i Pujol

Definition of test positivity: visual coloured band; the presence of any test line (T) indicates a positive result. Samples were applied directly to the test cassette and incubated for 15 min at room temperature before reading results with the naked eye, according to the manufacturer IFU

Blinding reported: unclear; presume only blinded to different Ags tests

"All Ag-RDT determinations were performed in parallel by two blinded technicians"

Timing of samples: N/A; all asymptomatic

Target condition and reference standard(s)	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Comparative	
Notes	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS

Baro 2021 [E]
Study characteristics

Patient Sampling	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Index tests	<p>Test name: [A] PanBio™ COVID-19 Ag Rapid test [B] CLINITEST Rapid COVID-19 Antigen Test [C] SD Biosensor SARS-CoV-2 Rapid Antigen Test [D] Lepu SARS-CoV-2 Antigen Rapid Test [E] Surescreen COVID-19 Coronavirus Rapid Antigen Test Cassette</p> <p>Manufacturer: [A] Abbott Rapid Diagnostics, Panbio Ltd, USA [B] Siemens Healthineers (Shanghai International Holding Corp), USA [C] Roche Diagnostics, SD Biosensor, Republic of Korea [D] Beijing Lepu Medical Technology Co., Ltd., China [E] SureScreen Diagnostics Ltd, UK</p> <p>Antibody: nucleocapsid protein</p> <p>Ag target: not reported</p> <p>Test method: [A] CGIA [B] Immunochromatographic [C] LFA (unclear)</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Baro 2021 [E] (Continued)

[D] CGIA

[E] LFA (unclear)

Samples used: NP (collected by HCW)

Transport media: VTM (DeltaSwab Virus, Deltalab; or UTM Universal Transport Medium, Copan)

Sample storage: samples stored for up to 24 h (2-8 °C) prior to RT-PCR then stored up to 12 h more at 2-8 °C until Ag testing

Test operator: lab technician at The University Hospital Germans Trias i Pujol

Definition of test positivity: visual coloured band; the presence of any test line (T) indicates a positive result. Samples were applied directly to the test cassette and incubated for 15 min at room temperature before reading results with the naked eye, according to the manufacturer IFU

Blinding reported: unclear; presume only blinded to different Ags tests

"All Ag-RDT determinations were performed in parallel by two blinded technicians"

Timing of samples: N/A; all asymptomatic

Target condition and reference standard(s)	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS
Comparative	
Notes	Comparative study of 5 Ag tests; Baro 2021 [A] reports full study characteristics and QUADAS

Basso 2021 [A]

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: COVID-19 inpatients (n = 138) and outpatients (n = 96) screened for suspected SARS-CoV-2 after contact with a SARS-CoV-2-positive person or with typical symptoms (n per group was not reported)</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): whole sample: 234 (87) Inpatients: 138 (84) Outpatients: 96 (3)</p>
Patient characteristics and setting	<p>Setting: inpatient and outpatient</p> <p>Location: Italy, University Hospital of Padova</p> <p>Country: Italy</p> <p>Dates: 1 August and 30 November, 2020</p> <p>Symptoms and severity: inpatients: 93/138 (67%) pneumonia, 97 (70%) fever > 37.5 °C, cough 46 (33%), dyspnoea 21 (15%) Outpatients: not reported</p> <p>Demographics: inpatients: 86, 62% male; mean age 56 years (SD 17); outpatients: 49, 51% male; mean age 42 years (SD 15)</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Basso 2021 [A] (Continued)

	Exposure history: not reported
Index tests	<p>Test name: [A] and [B] ESPLINE rapid test [C] Panbio COVID-19 Ag Rapid Test (A 3rd laboratory-based Ag detection assay was also evaluated but is not eligible for this review: LUMIPULSE SARS-CoV-2 Ag kit, Fujirebio, Tokyo, Japan)</p> <p>Manufacturer: [A] and [B] Fujirebio, Tokyo, Japan, [C] ABBOTT, Chicago, Illinois, USA</p> <p>Antibody: SARS-CoV-2 nucleocapsid protein</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] saliva self-sampling using Salivette device, SARSTEDT AG & Co, Nümbrecht, Germany; [B] and [C] NP swabs collected by qualified nurse</p> <p>Transport media: none used; NP swab testing conducted following manufacturer IFU</p> <p>Sample storage: all molecular and CLEIA Ag testing in both saliva and NP was performed in parallel within 3 h from collection</p> <p>Test operator: unclear; likely laboratory staff</p> <p>Definition of test positivity: not stated; visual inspection</p> <p>Blinding reported: unclear</p> <p>Timing of samples: inpatients (n = 138): 38, 27.6% ≤ 7 days pso; 74, 53.6% 7-14 days pso; 26, 18.8% > 14 days pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; TaqPath COVID-19 RT-PCR kit (Applied Biosystems, USA), performed by QuantStudio(TM) 5 Real-Time PCR Systems (Applied Biosystems, USA) and QuantStudio(TM) 5 RealTime PCR Systems (Applied Biosystems, USA) Threshold: ≥ 2 of 3 targets had an amplification plot with a Ct value of < 40</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): Orf1ab, N and S SARS-CoV-2 genes</p> <p>Samples used: saliva (aliquot from same sample as index test); NP paired swab</p> <p>Timing of reference standard: same as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p> <p>Time interval between index and reference tests: simultaneous; paired swab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes. Authors provided data underlying Figure 3 however number of samples tested per assay and sample type vary; reason given was insufficient material for some cases, the number discrepancy was stated as not due to test failure: [A] ESPLINE - saliva, n = 134 (55) [B] ESPINE - NP, n = 136 (64) [C] PanBio - NP, n = 116 (56) (Total of 164 (saliva) and 151 (NP) samples reported for LUMIPULSE)</p> <p>Uninterpretable results: none</p> <p>Indeterminate results (index test): none</p>

Basso 2021 [A] (Continued)

	Indeterminate results (reference standard): none
Flow and timing	<p>Time interval between index and reference tests: simultaneous; paired swab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes. Authors provided data underlying Figure 3 however number of samples tested per assay and sample type vary; reason given was insufficient material for some cases, the number discrepancy was stated as not due to test failure: [A] ESPLINE - saliva, n = 134 (55) [B] ESPINE - NP, n = 136 (64) [C] PanBio - NP, n = 116 (56) (Total of 164 (saliva) and 151 (NP) samples reported for LUMIPULSE)</p> <p>Uninterpretable results: none</p> <p>Indeterminate results (index test): none</p> <p>Indeterminate results (reference standard): none</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: no funding statement provided</p> <p>Publication status: published</p> <p>Source: Clinica Chimica Acta</p> <p>Author COI: no COI statement provided</p>

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 inclusions?	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?			High
DOMAIN 2: Index Test (Evaluations of single test application)			
Were the index test results interpreted without knowledge	Unclear		

Basso 2021 [A] (Continued)
 of the results of the reference
 standard?

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Basso 2021 [B]

Study characteristics

Patient Sampling	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] and [B] ESPLINE rapid test [C] Panbio COVID-19 Ag Rapid Test (A 3rd laboratory-based Ag detection assay was also evaluated but is not eligible for this review: LUMIPULSE SARS-CoV-2 Ag kit, Fujirebio, Tokyo, Japan)</p> <p>Manufacturer: [A] and [B] Fujirebio, Tokyo, Japan, [C] ABBOTT, Chicago, Illinois, USA</p> <p>Antibody: SARS-CoV-2 nucleocapsid protein</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] saliva self-sampling using Salivette device, SARSTEDT AG & Co, Nümbrecht, Germany; [B] and [C] NP swabs collected by qualified nurse</p> <p>Transport media: none used; NP swab testing conducted following manufacturer IFU</p> <p>Sample storage: all molecular and CLEIA Ag testing in both saliva and NP swabs performed in parallel within 3 h from collection</p> <p>Test operator: unclear; likely laboratory staff</p> <p>Definition of test positivity: not stated; visual inspection</p> <p>Blinding reported: unclear</p> <p>Timing of samples: inpatients (n = 138): 38, 27.6% ≤ 7 days pso; 74, 53.6% 7-14 days pso; 26, 18.8% > 14 days pso</p>
Target condition and reference standard(s)	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.

Basso 2021 [C]

Study characteristics

Basso 2021 [C] (Continued)

Patient Sampling	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] and [B] ESPLINE rapid test [C] Panbio COVID-19 Ag Rapid Test (A 3rd laboratory-based Ag detection assay was also evaluated but is not eligible for this review: LUMIPULSE SARS-CoV-2 Ag kit, Fujirebio, Tokyo, Japan)</p> <p>Manufacturer: [A] and [B] Fujirebio, Tokyo, Japan, [C] ABBOTT, Chicago, Illinois, USA</p> <p>Antibody: SARS-CoV-2 nucleocapsid protein</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] saliva self-sampling using Salivette device, SARSTEDT AG & Co, Nümbrecht, Germany; [B] and [C] NP swabs collected by qualified nurse</p> <p>Transport media: none used; NP swab testing conducted following manufacturer IFU</p> <p>Sample storage: all molecular and CLEIA Ag testing in both saliva and NP swabs performed in parallel within 3 h from collection</p> <p>Test operator: unclear; likely laboratory staff</p> <p>Definition of test positivity: not stated; visual inspection</p> <p>Blinding reported: unclear</p> <p>Timing of samples: inpatients (n = 138): 38, 27.6% ≤ 7 days pso; 74, 53.6% 7-14 days pso; 26, 18.8% > 14 days pso</p>
Target condition and reference standard(s)	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 tests using different types of samples; Basso 2021 [A] reports full study characteristics and QUADAS.

Beck 2021
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: all patients with signs and symptoms of COVID-19 presenting to an urgent care centre (n = 347)</p> <p>Recruitment: consecutive ("all patients")</p> <p>Prospective or retrospective: not stated; appears prospective</p>
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Beck 2021 (Continued)

	Sample size (cases): 347 (61)
Patient characteristics and setting	<p>Setting: urgent care centre</p> <p>Location: Advocate Aurora Health Urgent Care Center, West Bend, WI</p> <p>Country: USA</p> <p>Dates: not stated</p> <p>Symptoms and severity: all symptomatic; no further details</p> <p>Demographics: age range 1-90 years; ≤ 18 years 35.4%, 19-50 years 38.3%, > 50 years 26.2% of participants</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: SOFIA SARS Antigen FIA</p> <p>Manufacturer: Quidel</p> <p>Antibody: SARS-CoV</p> <p>Ag target: not reported</p> <p>Test method: FIA</p> <p>Samples used: nasal; collection not described but appears to be HCW ("providers" mentioned in acknowledgements). IFU describes NMT samples</p> <p>Transport media: none; "swabs were carefully returned to the paper envelope in which they came and were placed in a sealed plastic specimen transport bag"</p> <p>Sample storage: none; "specimens were delivered to the laboratory (located within the same building) within 10 minutes of collection"</p> <p>Test operator: lab staff</p> <p>Definition of test positivity: not stated; "tested ... according to the manufacturer's package insert"</p> <p>Blinding reported: yes; done first and in separate lab</p> <p>Timing of samples: ≤ 5 days pso 298, 86.1%; > 5 days pso 48, 13.9%</p>
Target condition and reference standard(s)	<p>Reference standard: transcription-mediated amplification (TMA); Hologic Aptima Panther SARS-CoV-2 TMA test. Cepheid Xpert Xpress SARS-CoV-2 RT-PCR used for discrepant samples (after approx. 3 weeks' frozen storage)</p> <p>Definition of non-COVID cases: as for cases</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP in Amies bacterial transport medium (Copan, Brescia, Italy)</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not stated; specimens were refrigerated and sent via courier to the central laboratory of ACL Laboratories</p> <p>Incorporated index test: no</p>
Flow and timing	Time interval between index and reference tests: simultaneous; paired swabs, NP collected first

Beck 2021 (Continued)

All participants received same reference standard: yes

Missing data: 1 sample only (low risk)

Uninterpretable results: 1 sample invalid on SOFIA

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported.

Discrepant analysis: 2/14 FNs were negative on Xpert Xpress; 1/1 FPs also negative Xpert Xpress

Unit of analysis: participant

Comparative

Notes

Funding: none reported

Publication status: published

Source: Journal of Clinical Microbiology

Author COI: none 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Beck 2021 (Continued)

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Billaud 2020
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity: teachers (n = 90) and students (n = 419) screened for COVID-19 as part of a cluster investigation (n = 509)

Recruitment: not stated; appears to be open to all

Prospective or retrospective: prospective

Patient characteristics and setting Setting: screening
 Location: college, Lyon
 Country: France

Dates: 16 and 17 September

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Billaud 2020 (Continued)

	<p>Symptoms and severity: 166/509, 32.6% symptomatic including 152/419 (36%) students</p> <p>Demographics: mean, median age Students 21.6 years, 21 years (18-37 years) Teachers 47.2 years, 49 years (26-64 years)</p> <p>Exposure history: outbreak investigation</p>
Index tests	<p>Test name: described as "ABBOTT SARS-COV2 Antigenic Test"; presumed to be Panbio COVID-19 Ag Test</p> <p>Manufacturer: Abbott</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP; collected by firefighters</p> <p>Transport media: none used</p> <p>Sample storage: N/A; tested immediately on site</p> <p>Test operator: not stated</p> <p>Definition of test positivity: visual line; as per manufacturer IFU</p> <p>Blinding reported: yes, performed first</p> <p>Timing of samples: not stated but includes people > 7 days pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; SARS-COV-2 (Thermofisher)</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP (paired)</p> <p>Timing of reference standard: as for index</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous</p> <p>All participants received same reference standard: yes</p> <p>Missing data: 47 missing, including 11 uninterpretable</p> <p>Uninterpretable results: 11 uninterpretable on Ag test</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: not stated, public funding</p>

Billaud 2020 (Continued)

Publication status: published

Source: report accessed via SFM Microbiologie website

Author COI: none

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			Unclear
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Billaud 2020 (Continued)

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

Blairon 2020

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: sampled from cohort of suspected COVID-19 patient samples sent for laboratory diagnosis (n = 56) (Excluded data for full cohort, as only those with negative Ag test underwent confirmatory RT-PCR; of 912 submitted samples during time period, 776 remained after removing repeat tests and were reported in main study)</p> <p>Recruitment: selection of 56 for verification analysis was not reported</p> <p>Prospective or retrospective: prospectively</p>
Patient characteristics and setting	<p>Setting: unclear; swabs obtained at hospital site, no further detail</p> <p>Location: not stated; author institution Iris Hospitals South, Brussels</p> <p>Country: Belgium</p> <p>Dates: 5 April-4 May 2020</p> <p>Symptoms and severity: not stated</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: COVID-19 Ag Respi-Strip (no product code reported)</p> <p>Manufacturer: Coris Bioconcept (Gembloux, Belgium)</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: LFA</p> <p>Samples used: NP swabs; collection not reported</p> <p>Transport media: samples for Ag testing taken from UTM-RT swabs (Copan spa, Brescia, IT)</p> <p>Sample storage: no storage described; infer that Ag test was conducted immediately on receipt of sample at on-site laboratory "after antigenic testing was performed, the molecular assessment of SARS-CoV-2 was outsourced to a university centre"</p>

Blairon 2020 (Continued)

	<p>Test operator: not stated; infer laboratory staff</p> <p>Definition of test positivity: as per manufacturer IFU</p> <p>Blinding reported: not stated; infer yes as conducted prior to PCR confirmation</p> <p>Timing of samples: not stated; appears to be on presentation (repeat tests ordered at clinician's discretion were excluded)</p>
Target condition and reference standard(s)	<p>Reference standard: qRT-PCR</p> <p>Definition of non-COVID cases: as above, single PCR negative to confirm absence of disease</p> <p>Genetic target(s): E gene</p> <p>Samples used: NP swabs (same as for Ag test)</p> <p>Timing of reference standard: not stated</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: not stated but infer short interval; samples sent to university centre laboratory for PCR confirmation</p> <p>All participants received same reference standard: yes (only if study author confirms Ag + also got PCR)</p> <p>Missing data: none reported; review team excluded main cohort data as no reference standard for Ag test-positive samples</p> <p>Uninterpretable results: none reported; 1 "invalid" sample excluded from main cohort</p> <p>Indeterminate results (index test): none reported; 1 "non-conform" sample excluded from main cohort</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: unclear; main cohort includes unique patient samples but not reported for separate group of 56</p>
Comparative	
Notes	<p>Funding: none to declare</p> <p>Publication status: published</p> <p>Source: Journal of Clinical Virology</p> <p>Author COI: none to declare</p>

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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Blairon 2020 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Blairon 2020 (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Bulilete 2021
Study characteristics

Patient Sampling	<p>Single-group multi-centre study estimating sensitivity and specificity Adults attending 1 of 4 primary health care or COVID-19 testing centres for PCR tests; included patients with symptoms suggestive of infection with referral by a GP, or close contact with a PCR-confirmed case 2 NP samples were collected, 1 for RT-PCR and the other was processed on site using the Panbio™ rapid antigen test kit for SARS-CoV-2</p> <p>Recruitment: consecutive patients > 18 years, attending the sites for RT-PCR testing</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 1362 (140); further 27 declined to participate</p>
Patient characteristics and setting	<p>Setting: 4 PHC centres and 2 COVID-EXPRESS test sites</p> <p>Location: Mallorca, Spain (Balearic Public Health Service)</p> <p>Country: Spain</p> <p>Dates: 2–25 October 2020</p> <p>Symptoms and severity: 680 (49.7%) reported symptoms < 7 days prior (most frequent: headache (341, 24.9%), sore throat (310, 22.6%), cough (301, 18.4%), and tiredness (251, 18.3%)). Asymptomatic: 689 (50.3%)</p> <p>Demographics: mean age 42.5 ± 14.9 years, and 744 (54.3%) women</p> <p>Exposure history: reasons for testing: 750 (54.8%) close contact with a confirmed positive COVID-19 individual, 503 (36.7% symptoms suggestive of COVID-19 and referral by a primary healthcare professional), 116 (8.5%) unknown</p>
Index tests	<p>Test name: Panbio COVID 19 antigen rapid test</p> <p>Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany</p> <p>Antibody: SARS-CoV-2 nucleocapsid protein</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: NP swabs by qualified nurse</p> <p>Transport media: none; immediate on site testing</p> <p>Sample storage: none reported; results were interpreted within 15 min following the manufacturer IFU</p> <p>Test operator: not stated; presume same qualified nurse</p> <p>Definition of test positivity: not stated</p>

Bulilete 2021 (Continued)

	Blinding reported: yes; test was conducted on site before PCR test Timing of samples: 967, 70.6% presented within 5 days of the onset of symptoms or close contact Symptomatic: 622/677, 92% within 7 days pso Asymptomatic: 481/688, 70% within 7 days contact, 173/688 unknown number of days
Target condition and reference standard(s)	Reference standard: rRT-PCR testing: MagMAX TM Viral/Pathogen Nucleic Acid Isolation Kit (ThermoFisher) and TaqPath TM COVID-19 CE-IVD RT-PCR Kit and QuantStudio TM (ThermoFisher); Ct threshold not reported Definition of non-COVID cases: as for cases; single negative Genetic target(s): ORF, N, and S Samples used: paired NP swab Timing of reference standard: same as for index; sample sent for processing within 24 h of collection Blinded to index test: not stated Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swab All participants received same reference standard: yes (7 PCR excluded; all Ag-ve) Missing data: yes Uninterpretable results: 3 RT-PCR with incorrect labelling; 16 Ag-RDT results missing Indeterminate results (index test): none reported Indeterminate results (reference standard): 4 inconclusive RT-PCR Unit of analysis: participant
Comparative	
Notes	Funding: no specific grant from funding agencies in the public, commercial or not-for-profit sectors Publication status: published Source: Journal of Infection 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Bulilete 2021 (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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?

Yes

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

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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?

No

Were the reference standard results interpreted without knowledge of the results of the index tests?

Unclear

Reference standard does not incorporate result of index test?

Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?

Yes

Did all patients receive the same reference standard?

Yes

Bulilete 2021 (Continued)

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Caruana 2021 [A]
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: all patients admitted to hospital (wards, intermediate care units and ICU) from the ED, with or without suspected SARS-CoV-2 infection (A second study investigating the correlation of symptom duration and variations in viral load was also reported, but not eligible for this review)</p> <p>Recruitment: consecutive; with target of 100 RT-PCR+ve and at least 200 RT-PCR-ve</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 572 (114)</p>
Patient characteristics and setting	<p>Setting: inpatient; patients admitted to hospital from the ED</p> <p>Location: Lausanne University hospital</p> <p>Country: Switzerland</p> <p>Dates: 6 November-6 December 2020</p> <p>Symptoms and severity: 239 (45%) asymptomatic, admitted for other reasons than COVID-19 suspicion; 293 (55%) symptoms consistent with COVID-19; included some with atypical symptoms (n not reported)</p> <p>Demographics: asymptomatic for COVID-19: age 67 years (IQR 49-81); 105, 44% female Symptomatic: age 75 years (IQR 61-85); 131 (45%) female</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: [A] STANDARD Q COVID-19 Rapid AgTest [B] PanbioTM COVID-19 Ag Rapid Test [C] One Step Immunoassay for Exdia COVID-19 Ag [D] BD Veritor System for Rapid Detection of SARS-CoV-2 [Result of STANDARD Q was used to guide care/triage pathway; patients and clinicians were blinded to the results of all other Ag tests]</p> <p>Manufacturer: [A] SD Biosensor - Republic of Korea /Roche - Switzerland [B] Abbott - USA [C] Precision Biosensor Inc. - Republic of Korea [D] Becton Dickinson - USA</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: NP (collection not reported)</p>

Caruana 2021 [A] (Continued)

Transport media: wet swab procedure: NP swabs suspended in 2.5-3 mL VTM, then **[A] 350 µL of sample mixed with buffer solution** [B], [C] and [D] 300 µL of sample mixed with buffer solution

Sample storage: NP delivered to the RAT lab, immediately after the sampling procedure

Test operator: laboratory technicians

Definition of test positivity: **[A] and [B] visually** [C] and [D] automatically using analyser

Blinding reported: presumed (based on timing of tests)

Timing of samples: ≤ 4 days: 138/293 (47%); 4-7 days: 46/293 (16%); ≥ 7 days: 44/293 (15%)
Missing data/not typical COVID-19 symptoms: 65/293 (22%)

Target condition and reference standard(s)

Reference standard: RT-PCR; assay used varied according to result of STANDARD Q test
'Classical' RT-PCR used for RDT+ve symptomatic cases and for RDT-ve asymptomatic patients: either
[1] test Cobas 6800 SARS-CoV-2 (Roche, Basel, Switzerland) or
[2] automated high-throughput molecular diagnostic (MDx) platform
'Rapid' RT-PCR used for RDT-ve symptomatic cases and for RDT+ve asymptomatic patients: either
[3] VIASURE SARS-CoV-2 (N1 + N2) Real Time PCR Detection Kit for BD MAX (Becton Dickinson, USA), or
[4] GeneXpert SARS-CoV-2 test (Cepheid, www.cepheid.com)
Viral load was quantified using the equation: $VL = (10^{-(Ct - 40.856)} / -3.697) * 100$, derived from RNA quantification

Definition of non-COVID cases: as for cases

Genetic target(s): [D] E- and RdRp- encoding genes
[A] to [C] not reported

Samples used: same as for index test (same swab)

Timing of reference standard: same as for index test

Blinded to index test: no; assay used varied according to symptom status and RDT result

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab

All participants received same reference standard: yes; all RT-PCR

Missing data: yes; 67 excluded including 40 with missing results

Uninterpretable results: not reported

Indeterminate results (index test): n = 27 invalid RAT results

Indeterminate results (reference standard): not reported

Comparative

Notes

Funding: no financial support

Publication status: published

Source: Microbiology

Author COI: from published version: "Croxatto reports grants from Becton Dickinson outside the submitted work. Greub reports grants from Resistell, from Nittobo, outside the submitted work

Caruana 2021 [A] (Continued)

and he is the co-director of “JeuPro,” a start-up distributing the game Krobs, a card game about microbe transmission.”

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	No		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Caruana 2021 [A] *(Continued)*

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Caruana 2021 [B]
Study characteristics

Patient Sampling Comparative study of 4 Ag tests; [Caruana 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 4 Ag tests; [Caruana 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Test name: [A] STANDARD Q COVID-19 Rapid Antigen Test
[B] Panbio™ COVID-19 Ag Rapid Test
 [C] One Step Immunoassay for Exdia COVID-19 Ag
 [D] BD Veritor System for Rapid Detection of SARS-CoV-2
 (Result of STANDARD Q was used to guide care/triage pathway; patients and clinicians were blinded to the results of all other Ag tests)

Manufacturer: [A] SD Biosensor - Republic of Korea /Roche - Switzerland
[B] Abbott - USA
 [C] Precision Biosensor Inc. - Republic of Korea
 [D] Becton Dickinson - USA

Antibody: not reported

Ag target: not reported

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Caruana 2021 [B] (Continued)

Test method: not reported

Samples used: NP (collection not reported)

Transport media: wet swab procedure: NP swabs suspended in 2.5-3 mL VTM, then
[A] 350 µL of sample mixed with buffer solution

[B], [C] and [D] 300 µL of sample mixed with buffer solution

Sample storage: NP delivered to the RAT lab, immediately after the sampling procedure

Test operator: laboratory technicians

Definition of test positivity: **[A] and [B] visually**
[C] and [D] automatically using analyser

Blinding reported: presumed (based on timing of tests)

Timing of samples: ≤ 4 days: 138/293 (47%); 4-7 days: 46/293 (16%); ≥ 7 days: 44/293 (15%)
Missing data/not typical COVID-19 symptoms: 65/293 (22%)

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.

Caruana 2021 [C]

Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] STANDARD Q COVID-19 Rapid Antigen Test [B] Panbio™ COVID-19 Ag Rapid Test [C] One Step Immunoassay for Exdia COVID-19 Ag [D] BD Veritor System for Rapid Detection of SARS-CoV-2 (Result of STANDARD Q was used to guide care/triage pathway; patients and clinicians were blinded to the results of all other Ag tests)</p> <p>Manufacturer: [A] SD Biosensor - Republic of Korea /Roche - Switzerland [B] Abbott - USA [C] Precision Biosensor Inc. - Republic of Korea [D] Becton Dickinson - USA</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: NP (collection not reported)</p> <p>Transport media: wet swab procedure: NP swabs suspended in 2.5-3 mL VTM, then</p>

Caruana 2021 [C] (Continued)

[A] 350 µL of sample mixed with buffer solution

[B], [C] and [D] 300 µL of sample mixed with buffer solution

Sample storage: NP delivered to the RAT lab, immediately after the sampling procedure

Test operator: laboratory technicians

Definition of test positivity: [A] and [B] visually

[C] and [D] automatically using analyser

Blinding reported: presumed (based on timing of tests)

Timing of samples: ≤ 4 days: 138/293 (47%); 4-7 days: 46/293 (16%); ≥ 7 days: 44/293 (15%)

Missing data/not typical COVID-19 symptoms: 65/293 (22%)

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.

Caruana 2021 [D]

Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] STANDARD Q COVID-19 Rapid Antigen Test [B] Panbio™ COVID-19 Ag Rapid Test [C] One Step Immunoassay for Exdia COVID-19 Ag [D] BD Veritor System for Rapid Detection of SARS-CoV-2 (Result of STANDARD Q was used to guide care/triage pathway; patients and clinicians were blinded to the results of all other Ag tests)</p> <p>Manufacturer: [A] SD Biosensor - Republic of Korea /Roche - Switzerland [B] Abbott - USA [C] Precision Biosensor Inc. - Republic of Korea [D] Becton Dickinson - USA</p> <p>Antibody: not reported Ag target: not reported Test method: not reported Samples used: NP (collection not reported)</p> <p>Transport media: wet swab procedure: NP swabs suspended in 2.5-3 mL VTM, then [A] 350 µL of sample mixed with buffer solution [B], [C] and [D] 300 µL of sample mixed with buffer solution</p> <p>Sample storage: NP delivered to the RAT lab, immediately after the sampling procedure</p>

Caruana 2021 [D] *(Continued)*

Test operator: laboratory technicians

 Definition of test positivity: [A] and [B] visually
[C] and [D] automatically using analyser

Blinding reported: presumed (based on timing of tests)

Timing of samples: ≤ 4 days: 138/293 (47%); 4-7 days: 46/293 (16%); ≥ 7 days: 44/293 (15%)

Missing data/not typical COVID-19 symptoms: 65/293 (22%)

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Caruana 2021 [A] reports full study characteristics and QUADAS.

Cerutti 2020
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity in 2 cohorts: (1) symptomatic patients attending one of 2 EDs (n = 185) (2) asymptomatic travellers returning home from European high-risk countries (Croatia, Spain, Malta) (n = 145)</p> <p>Recruitment: (1) random; (2) not stated, presume consecutive</p> <p>Prospective or retrospective: not stated</p>
Patient characteristics and setting	<p>Setting: mixed; (1) ED; (2) possible contacts</p> <p>Location: (1) 2 infectious disease reference centres in northern Italy (ASL Città di Torino, Turin and San Martino University Hospital, Genoa); (2) not stated; samples sent to Microbiology and Virology Laboratory, Amedeo di Savoia Hospital, Torino</p> <p>Country: Italy</p> <p>Dates: (1) 3 March-1 May; (2) August 2020</p> <p>Symptoms and severity: not stated; cohort (2) were asymptomatic</p> <p>Demographics: (1) mean age 44.6, 95% CI 40.7-48.6; (2) mean age 35.9, 95% CI 32.7-39.1</p> <p>Exposure history: (1) not stated; (2) high-risk country visit</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag</p> <p>Manufacturer: SD-Biosensor, RELAB, I</p> <p>Antibody: NP</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP; collection not stated</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Cerutti 2020 (Continued)

	<p>Transport media: UTM (Copan, I)</p> <p>Sample storage: primarily run in parallel with standard care RT-PCR; 13 were frozen residual samples</p> <p>Test operator: not stated; laboratory staff presumed</p> <p>Definition of test positivity: visual line after 15-30 min; as per manufacturer IFU</p> <p>Blinding reported: not stated</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Seegene Allplex 2019 n-CoV Assay (n = 159), DiaSorin Simplexa (n = 28), and Cobas 6800 Roche (n = 118)</p> <p>Definition of non-COVID cases: single negative</p> <p>Genetic target(s): not stated</p> <p>Samples used: not stated; seems to be same as index</p> <p>Timing of reference standard: not stated</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous; not clear if same sample used or paired swabs obtained</p> <p>All participants received same reference standard: yes; different assays</p> <p>Missing data: none reported; no participant flow diagram reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: RELab donated the STANDARD Q COVID-19 SD-Biosensor kits used</p> <p>Publication status: published</p> <p>Source: Journal of Clinical Virology</p> <p>Author COI: the authors report no declarations of interest.</p>

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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Cerutti 2020 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Cerutti 2020 (Continued)

Could the patient flow have introduced bias?

Unclear risk

Chaimayo 2020
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: suspected cases of COVID-19 including symptomatic and contact individuals, including travellers, quarantined individuals and pre-operative patients</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: not stated</p> <p>Sample size (cases): 60 (37)</p>
Patient characteristics and setting	<p>Setting: mixed</p> <p>Location: not all specified; main institute was Siriraj Hospital, Bangkok, Thailand</p> <p>Country: Thailand</p> <p>Dates: March-May 2020</p> <p>Symptoms and severity: PCR+: 37/60, 61.7% showed signs and symptoms of upper respiratory tract infection 5 (8.3%) pneumonia and ICU admission, 11 fever, 4 unspecified, 3 asymptomatic. NB - supplementary file shows 53/60 with fever</p> <p>Demographics: PCR+: median age 38.5 years (range 21–72); 36 (60%) male PCR–: median age 61 years (range 16–95); 163/394 (41%) male</p> <p>Exposure history: PCR+: 45, 75% direct contact with confirmed cases, including family and friends (30%; n = 18), karaoke bars and pubs (23.3%; n = 14), boxing stadiums (18.3%; n = 11), taxi drivers (1.7%; n = 1), workplace peers (1.7%; n = 1)</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag kit</p> <p>Manufacturer: SD Biosensor, Republic of Korea</p> <p>Antibody: SARS-CoV-2 nucleocapsid (N) antigen</p> <p>Ag target: mouse monoclonal anti-SARS-CoV-2 antibody against SARS-CoV-2 N antigen</p> <p>Test method: CGIA</p> <p>Samples used: mixed; 447 NP or throat swabs, 4 endotracheal aspirates (tracheal suction), 3 sputum</p> <p>Transport media: 2 mL VTM; Hanks' balanced salt, 0.4% fetal bovine serum, HEPES, antibiotic and antifungal agents</p> <p>Sample storage: transported at 2–8 °C to the Microbiology laboratory, Siriraj Hospital, for processing within a few hours</p> <p>Test operator: not stated; likely laboratory staff, "All specimens were processed in biosafety level-3 (BSL-3) and biosafety level-2 enhanced (BSL-2+) facilities with full personal protective equipment"</p> <p>Definition of test positivity: for positive COVID-19 Ag result, 2 coloured lines of control (C) and test (T) lines were presented.</p>

Chaimayo 2020 (Continued)

	Blinding reported: not mentioned Timing of samples: PCR+: 3 asymptomatic, 41 (68%) day 1-7, 12 (20%) day > 7, 4 unspecified time pso
Target condition and reference standard(s)	Reference standard: RT-PCR; Allplex™ 2019-nCoV Assay (Seegene, Korea); Ct value < 40 for all 3 target genes was defined as a positive result Definition of non-COVID cases: as for cases; single negative Genetic target(s): E gene (Sarbecovirus), and RdRp and N genes (SARS-CoV-2) Samples used: NP swab in VTM Timing of reference standard: as for index test Blinded to index test: not stated Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swab All participants received same reference standard: yes Missing data: none stated Uninterpretable results: none reported Indeterminate results (index test): none Indeterminate results (reference standard): none Unit of analysis: participant
Comparative	
Notes	Funding: "partly supported by Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand through grant number R016034012" Publication status: published Source: Virology Journal Author COI: 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 inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	

Chaimayo 2020 (Continued)

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

High

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

High

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Chaimayo 2020 (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Unclear risk

Ciotti 2021
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: NP swabs from patients with suspected SARS-CoV-2 infection at the ED or Infectious Diseases ward</p> <p>Recruitment: not reported</p> <p>Prospective or retrospective: not reported</p> <p>Sample size (cases): 50 (39)</p>
Patient characteristics and setting	<p>Setting: mixed; ED or Infectious Diseases ward</p> <p>Location: University Hospital Tor Vergata, Rome</p> <p>Country: Italy</p> <p>Dates: May-September 2020</p> <p>Symptoms and severity: not reported</p> <p>Demographics: median age 53.5 years, (mean 53.1; range: 15–94 years); 24, 48% male</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: COVID-19 Ag Respi-Strip</p> <p>Manufacturer: Coris BioConcept</p> <p>Antibody: nucleoprotein of SARS-CoV and SARS-CoV-2</p> <p>Ag target: monoclonal antibodies</p> <p>Test method: CGIA</p> <p>Samples used: NP (collection not described)</p> <p>Transport media: not clear but seems that no VTM used; 100 µL "nasopharyngeal secretions are mixed with four drops (about 100 µL) of lysis buffer"</p> <p>Sample storage: none reported</p> <p>Test operator: not stated; virology laboratory</p> <p>Definition of test positivity: visual appearance of test and control (red) lines</p> <p>Blinding reported: not stated</p> <p>Timing of samples: not reported</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Allplex 2019n-CoV assay</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Ciotti 2021 (Continued)

Definition of non-COVID cases: as for cases; single negative

Genetic target(s): E gene (Sarbecovirus sub-genus) and N and RdRp genes (SARS-CoV-2)

Samples used: NP swabs

Timing of reference standard: not stated; same as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous; appears to be same swab but not clearly stated

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis

Comparative

Notes

Funding: no funding statement reported

Publication status: published

Source: Journal of Medical Virology

Author COI: the authors declare that there are no conflict of interests

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Ciotti 2021 (Continued)

If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Courtellemont 2021
Study characteristics

Patient Sampling	<p>Unclear design estimating sensitivity and specificity (coded as 2-group because of deliberate sampling of PCR+ve cases):</p> <p>(1) symptomatic (headache, fatigue, fever, or respiratory signs) or asymptomatic people voluntarily accessing the COVID-19 Screening Department (n = 231)</p> <p>(2) hospitalized SARS-CoV-2-positive patients (n = 17)</p> <p>(review team excluded 20 cases with a previous positive RT-qPCR within 5 days but a negative RTqPCR at the time of study sampling.)</p>
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Courtellemont 2021 (Continued)

	<p>Recruitment: unclear</p> <p>Prospective or retrospective: unclear</p>
Patient characteristics and setting	<p>Setting: mixed</p> <p>Location: COVID-19 Screening Department and SARS CoV-2-positive patients hospitalized in the Infectious Diseases Department of the Centre Hospitalier Régional (CHR) of Orléans, France, or the Department of Infectious and Tropical Diseases of the Centre Hospitalier Universitaire (CHU) Tenon, Paris</p> <p>Country: France</p> <p>Dates: 12-19 October</p> <p>Symptoms and severity: 99/121, 82% cases were symptomatic; 22 asymptomatic</p> <p>Demographics: median age 38 years, mean age 43 years (range: 18-96), 117, 47% male</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: COVID-VIRO</p> <p>Manufacturer: AAZ, Boulogne Billancourt, France</p> <p>Antibody: nucleocapsid</p> <p>Ag target: monoclonal</p> <p>Test method: CGIA</p> <p>Samples used: NP; collected by trained personnel (nurse, doctors, or biologist); subgroup also had OP or saliva collected</p> <p>Transport media: direct testing for Ag test</p> <p>Sample storage: none</p> <p>Test operator: not stated</p> <p>Definition of test positivity: visible line; as per manufacturer IFU</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 5 days pso, mean 5.3 days, range 1-20d</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; TaqPath Covid-19 Multiplex RT-PCR, Thermofisher</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): ORF1ab, S and N genes</p> <p>Samples used: NP in VTM; paired</p> <p>Timing of reference standard: as for index</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous; paired</p> <p>All participants received same reference standard: yes</p>

Courtellemont 2021 (Continued)

Missing data: none reported, no participant flow diagram reported; review team excluded 20 cases with a previous positive RT-qPCR within 5 days but a negative RTqPCR at the time of study sampling

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: no funding statement reported

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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			Unclear
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			

Courtellemont 2021 (Continued)

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Del Vecchio 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: patients with and without symptoms examined at ED (n = 1153), infectious disease wards (n = 279) or other department (n = 9) who required COVID-19 testing either due to a) presence of COVID-19-related symptoms (fever and/or cough and/or headache, diarrhoea, asthenia, muscle pain, joint pain, loss of taste or smell, or shortness of breath, with or without pneumonia); or b) asymptomatic but had a contact with a confirmed case of SARS-CoV-2 infection during the previous 10 days</p> <p>Recruitment: convenience, only included if both Ag and PCR results were available</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 1441 (61); 58/61 PCR+ were observed at ED</p>
Patient characteristics and setting	<p>Setting: mixed; ED and infectious disease ward admissions</p> <p>Location: University Hospital of Padua</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Del Vecchio 2021 (Continued)

Country: Italy

Dates: 15 September-16 October 2020

Symptoms and severity: only reported for PCR+:

51/61 (84%) symptomatic, including 10 (20%) with asthenia, 7 (14%) with cough, 3 (6%) with dyspnoea (1/3 severe), 32 (63%) with fever, 7 (14%) with headache

Demographics: 760 (53%) male

Age: 0-19 years: n = 54, 20-39 years: n = 247, 40-59 years: n = 262, 60-79 years: n = 420, 80-99 years: n = 457, > 100 years: n = 1

Exposure history: not reported

Index tests

Test name: Panbio COVID-19 Ag Rapid Test Device

Manufacturer: Abbott Lake Country, IL, USA

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: not stated; mentions NP in Discussion only

Transport media: not used for Ag testing

Sample storage: processed right after sampling; maximum 1-h delay

Test operator: not stated

Definition of test positivity: according to manufacturer IFU

Blinding reported: yes; conducted first

Timing of samples: 0-7 days: n = 39, 64% (28 day 0-3); 8-14 days: n = 11, 18%; ≥ 15 days: n = 1

Target condition and reference standard(s)

Reference standard: RT-PCR; DiaSorin Molecular Simplexa COVID-19 Direct assay system (Diasorin Cypress, CA, USA)

"Samples showing a positive result for both viral targets were considered positive. Samples with either a single positive target or with Ct value ≥ 30 were confirmed with an in-house real-time RT-PCR targeting the N2 gene."

Definition of non-COVID cases: as for cases

Genetic target(s): S gene and the ORF1ab gene

Samples used: not stated

Timing of reference standard: as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous; paired swabs

All participants received same reference standard: yes

Missing data: none reported (1849 patients only had either RAT or RT-PCR test results available and were excluded a priori)

Uninterpretable results: none reported

Del Vecchio 2021 (Continued)

Indeterminate results (index test): none reported
 Indeterminate results (reference standard): none reported
 Unit of analysis: participant

Comparative

Notes Funding: "COVID-19 emergency fund from University of Padova to ST"
 Publication status: preprint (not peer reviewed)
 Source: medRxiv
 Author COI: 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?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			Unclear
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			

Del Vecchio 2021 (Continued)

Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Dominguez Fernandez 2021
Study characteristics

Patient Sampling	Unclear design estimating sensitivity and specificity: users with symptoms compatible with COVID-19 and/or were close contacts of users with a positive COVID-19 diagnosis Recruitment: not stated Prospective or retrospective: not stated Sample size (cases): 30 (20)
Patient characteristics and setting	Setting: care home Location: not stated; author institutions included the Coordination and Assistance Support Unit for Social and Health Residences of the A Coruna and Cee Health Area and the Microbiology Service, A Coruna University Hospital Complex, A Coruna

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Dominguez Fernandez 2021 (Continued)

Country: Spain

Dates: September 2020

Symptoms and severity: 90% had symptoms compatible with SARS-CoV-2 infection of < 5 days of evolution and the other 10% were asymptomatic, but were close contacts

Demographics: mean age 76.2 years (SD: 19.76), 36.7% male

Exposure history: 10% asymptomatic close contacts

Index tests

Test name: Panbio COVID-19 Ag Rapid Test Device

Manufacturer: Abbott

Antibody: not reported

Ag target: not reported

Test method: CGIA

Samples used: not stated

Transport media: not stated

Sample storage: not stated

Test operator: not stated

Definition of test positivity: not stated

Blinding reported: not stated

Timing of samples: 90% were < 5 days pso

Target condition and reference standard(s)

Reference standard: RT-PCR; no further details

Definition of non-COVID cases: single negative

Genetic target(s): not stated

Samples used: not stated

Timing of reference standard: not stated

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous; not stated whether paired/same sample used

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Dominguez Fernandez 2021 (Continued)

Comparative

Notes

Funding: no funding statement reported

Publication status: published letter

Source: Enfermedades Infecciosas y Microbiología Clínica

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		

Dominguez Fernandez 2021 (Continued)

Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Drain 2021(a)
Study characteristics

Patient Sampling	<p>Report of 2 studies estimating sensitivity and specificity, 1st is a 2-group study using nasal swabs and the 2nd a single-group study using NP swabs.</p> <p>[1] nasal swabs from children and adults presenting for COVID-19 testing at 10 sites in the USA and UK (first time period)</p> <p>[2] nasal swab samples from a commercial supplier (MRN Diagnostics, Florida, USA) and also collected from an at-risk population (LumiraDx Stirling, UK)</p> <p>[3] NP swabs from children and adults presenting for COVID-19 testing at 10 sites in the USA and UK (second time period)</p> <p>Data for cohort [1] and [2] are included as Drain 2021(a); see Drain 2021(b) for details of cohort [3]</p> <p>Recruitment: unclear</p> <p>Prospective or retrospective: described as prospective</p> <p>Sample size (cases): 257(83)</p>
Patient characteristics and setting	<p>Setting: presume COVID-19 testing centres</p> <p>Location: 10 sites in the UK and USA</p> <p>Country: UK and USA</p> <p>Dates: [1] 26 June-23 July 2020; [2] not reported</p> <p>Symptoms and severity: whole sample: 414/512 (81%) symptomatic; [1]+[2] 159/257 (62%) symptomatic</p> <p>Demographics: whole sample: 287 female, 225 male.</p> <p>Age (0-90 years); [1]+[2] mean age 34 years (SD 15.7 years); 142 (55%) female</p> <p>Exposure history: not stated</p>

Drain 2021(a) (Continued)

Index tests	Test name: LumiraDx SARS-CoV-2 Manufacturer: LumiraDx UK Ltd. Antibody: N Ag target: not stated Test method: microfluidic immunoassay with fluorescent latex signal Samples used: [1]+[2] AN; at 8 of 10 sites, swabs collected and tested by minimally trained operators Transport media: none; 0.7 mL of a proprietary extraction buffer for LumiraDx SARS-CoV-2 Ag test Sample storage: [1] tested fresh and then frozen within 1 h of collection [2] Unclear Test operator: unclear; included minimally trained operators Definition of test positivity: result shown on touchscreen as "positive" Blinding reported: [1]+[2] results from retested frozen samples were described as blinded Timing of samples: [1]+[2] range 1-12 days; mean 4.0 days (SD 2.9 days) pso
Target condition and reference standard(s)	Reference standard: RT-PCR; SARS-CoV-2 assay using a Roche Cobas 6800 platform (Roche Molecular Diagnostics, Indianapolis, IN, USA); threshold Ct of 35 (based on Figure 2) Definition of non-COVID cases: single negative PCR Same as for cases; appears to be single negative PCR to confirm absence of infection Genetic target(s): not stated Samples used: paired swab Timing of reference standard: same as for index test Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneously All participants received same reference standard: yes Missing data: not mentioned Uninterpretable results: not mentioned Indeterminate results (index test): not mentioned Indeterminate results (reference standard): not mentioned Unit of analysis: participant
Comparative	
Notes	Funding: "work was supported by LumiraDx Ltd, including funding of the journal's Rapid Services fee" Publication status: published paper

Drain 2021(a) *(Continued)*

Source: academic journal

Author COI: 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Drain 2021(a) *(Continued)*

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Drain 2021(b)
Study characteristics

Patient Sampling	<p>Report of 2 studies estimating sensitivity and specificity, 1st is a 2-group study using nasal swabs and the 2nd a single-group study using NP swabs: [1] nasal swabs from children and adults presenting for COVID-19 testing at 10 sites in the USA and UK (first time period) [2] nasal swab samples from a commercial supplier (MRN Diagnostics, Florida, USA) and also collected from an at-risk population (LumiraDx Stirling, UK) [3] NP swabs from children and adults presenting for COVID-19 testing at 10 sites in the USA and UK (second time period) See Drain 2021(a) for details of cohort [1] and [2]; Data for cohort [3] included as Drain 2021(b)</p> <p>Recruitment: unclear</p> <p>Prospective or retrospective: described as prospective</p> <p>Sample size (cases): 255 (40)</p>
Patient characteristics and setting	<p>Setting: presume COVID-19 testing centres</p> <p>Location: 10 sites in the UK and USA</p> <p>Country: UK and USA</p> <p>Dates: [3] 17 August-28 September 2020</p> <p>Symptoms and severity: whole sample: 414/512 (81%) symptomatic [3] 255/255 (100%) symptomatic</p> <p>Demographics: whole sample: 287 female, 225 male. Age (0-90 years) [3] mean age 33.2 years (SD 19.4 years); 145 (57%) female</p>

Drain 2021(b) (Continued)

	Exposure history: not stated
Index tests	<p>Test name: LumiraDx SARS-CoV-2</p> <p>Manufacturer: LumiraDx UK Ltd</p> <p>Antibody: N</p> <p>Ag target: not stated</p> <p>Test method: microfluidic immunoassay with fluorescent latex signal</p> <p>Samples used: [3] NP; at 8 of 10 sites, swabs collected and tested by minimally trained operators</p> <p>Transport media: none; 0.7 mL of a proprietary extraction buffer for LumiraDx SARS-CoV-2 Ag test</p> <p>Sample storage: [3] no storage</p> <p>Test operator: unclear; included minimally trained operators</p> <p>Definition of test positivity: result shown on touchscreen as "positive"</p> <p>Blinding reported: [3] yes, based on timing of test</p> <p>Timing of samples: whole sample: range 1-12 days [3] mean 3.5 days (SD 2.5) pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; SARS-CoV-2 assay using a Roche Cobas 6800 platform (Roche Molecular Diagnostics, Indianapolis, IN, USA); threshold Ct of 35 (based on Figure 2)</p> <p>Definition of non-COVID cases: same as for cases; appears to be single negative PCR to confirm absence of infection</p> <p>Genetic target(s): not stated</p> <p>Samples used: paired swab</p> <p>Timing of reference standard: same as for index test</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneously</p> <p>All participants received same reference standard: yes</p> <p>Missing data: not mentioned</p> <p>Uninterpretable results: not mentioned</p> <p>Indeterminate results (index test): not mentioned</p> <p>Indeterminate results (reference standard): not mentioned</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	Funding: "work was supported by LumiraDx Ltd, including funding of the journal's Rapid Services fee"

Drain 2021(b) (Continued)

Publication status: published paper

Source: academic journal

Author COI: 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		

Drain 2021(b) *(Continued)*

Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Drevinek 2020 [A]
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: participants aged ≥ 10 years, who attended a COVID-19 testing centre due to suspicion of COVID-19 (n = 273) or contact tracing (n = 290); either referred by a GP or public health officer (n = 511) or were 'self-payers' (n = 54)</p> <p>Recruitment: not stated but seems to be all who consented to participate during stated time period</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 591 (223)</p>
Patient characteristics and setting	<p>Setting: COVID-19 testing site at a university hospital</p> <p>Location: Motol University Hospital, Prague</p> <p>Country: Czech Republic</p> <p>Dates: 4-day period in October 2020</p> <p>Symptoms and severity: 290 (49%) symptomatic on day of testing</p> <p>Demographics: mean age 40 years (range 12-78 years); 44.7% male</p> <p>Exposure history: 290 tested as a result of contact tracing</p>
Index tests	<p>Test name: [A] Panbio Covid-19 Ag Rapid Test [B] STANDARD F Covid-19 Ag FIA</p> <p>Manufacturer: [A] Abbott, Germany [B] SD Biosensor, Republic of Korea</p>

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Drevinek 2020 [A] (Continued)

Antibody: not stated

Ag target: not stated

Test method: **[A] CGIA**
[B] FIA

Samples used: NP swabs (1 per Ag assay); collection not described

Transport media: none used; states "without the optional step of inserting the swab into the viral transport medium"

Sample storage: no storage; tested immediately on collection

Test operator: not stated

Definition of test positivity: **[A] visual assessment after 15 min incubation**
[B] STANDARD F200 Analyser (in 'read-only' mode) after 30 min incubation

Blinding reported: not stated, but very likely considering test was done prior to reference standard
Yes; conducted first

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: RT-PCR; Allplex 2019n-CoV assay
Ct value < 40 for positive result

Definition of non-COVID cases: as for cases; single negative

Genetic target(s): N, E and RdRP/S genes

Samples used: combined NP + OP swab in VTM

Timing of reference standard: not stated; same as for index

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous; paired swab

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: "supported by the Ministry of Health of the Czech Republic - conceptual development of research organization Motol University Hospital, FNM"

Publication status: published

Source: medRxiv

Author COI: no conflicts of interest to report

Drevinek 2020 [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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

Drevinek 2020 [A] *(Continued)*

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Unclear

Could the patient flow have introduced bias?

Unclear risk

Drevinek 2020 [B]
Study characteristics

Patient Sampling Comparative study of 2 Ag tests; [Drevinek 2020 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 2 Ag tests; [Drevinek 2020 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Test name: [A] Panbio Covid-19 Ag Rapid Test
[B] STANDARD F Covid-19 Ag FIA

Manufacturer: [A] Abbott, Germany
[B] SD Biosensor, Republic of Korea

Antibody: not stated

Ag target: not stated

Test method: [A] CGIA
[B] FIA

Samples used: NP swabs (1 per Ag assay); collection not described

Transport media: none used; states "without the optional step of inserting the swab into the viral transport medium"

Sample storage: no storage; tested immediately on collection

Test operator: not stated

Definition of test positivity: [A] visual assessment after 15 min incubation
[B] Standard F200 Analyser (in 'read-only' mode) after 30 min incubation

Blinding reported: not stated, but very likely considering test was done prior to reference standard
 Yes; conducted first

Timing of samples: not stated

Drevinek 2020 [B] *(Continued)*

Target condition and reference standard(s)	Comparative study of 2 Ag tests; Drevinek 2020 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 Ag tests; Drevinek 2020 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 Ag tests; Drevinek 2020 [A] reports full study characteristics and QUADAS.

Faico-Filho 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: adults (aged > 18 years) treated in the ED and hospitalized for at least 24 h, including those</p> <ol style="list-style-type: none"> 1. with COVID-19 related symptoms and/or contact with a confirmed case 2. decompensation of underlying disease, or 3. suggestive CT findings (ground glass) <p>Recruitment: not reported; implies all eligible were included</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 127 (70)</p>
Patient characteristics and setting	<p>Setting: ED</p> <p>Location: São Paulo Hospital in São Paulo</p> <p>Country: Brazil</p> <p>Dates: not reported</p> <p>Symptoms and severity: not reported</p> <p>Demographics: mean age (SD): 60 (17.5) years Sex: 69/127 (54%) male</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Panbio COVID-19 Ag test</p> <p>Manufacturer: Abbott</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: NP (not reported who collected by)</p> <p>Transport media: not reported</p> <p>Sample storage: only reported that NP swab samples were simultaneously tested with both index and reference tests and RT-PCR results were available within 6-24 h</p>

Faico-Filho 2021 (Continued)

	<p>Test operator: not reported</p> <p>Definition of test positivity: according to manufacturer</p> <p>Blinding reported: not reported</p> <p>Timing of samples: mean days pso: 5 (4; 7)</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; [1] GeneFinder COVID-19 Plus RealAmp Kit (OSANG Healthcare Co., Ltd.); [2] Mobius XGEN MASTER COVID-19 test for inconclusive GeneFinder results</p> <p>Definition of non-COVID cases: as for cases</p> <p>Genetic target(s): [1] RdRp, E and N SARS-CoV-2 genes [2] ORF1ab and N SARS-CoV-2 genes</p> <p>Samples used: NP</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not reported</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous</p> <p>All participants received same reference standard: yes</p> <p>Missing data: not reported</p> <p>Uninterpretable results: not reported</p> <p>Indeterminate results (index test): not reported</p> <p>Indeterminate results (reference standard): not reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "the UNIFESP team received Panbio COVID-19 Ag tests for the study from Abbott."</p> <p>Publication status: preprint (not peer reviewed)</p> <p>Source: medRxiv</p> <p>Author COI: "the UNIFESP team received Panbio COVID-19 Ag tests for the study from Abbott. Dr. Nancy Bellei provides lectures for and is on the advisory board of Abbott."</p>

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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Faico-Filho 2021 (Continued)

Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Faico-Filho 2021 (Continued)

Could the patient flow have introduced bias?

Unclear risk

Favresse 2021 [A]
Study characteristics

Patient Sampling	<p>Single-group estimating sensitivity and specificity: NP samples from patients who presented for SARS-CoV-2 testing at single institution</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: not stated</p> <p>Sample size (cases): 188 (96)</p>
Patient characteristics and setting	<p>Setting: laboratory-based</p> <p>Location: laboratory of the Clinique Saint-Luc (Bouge, Namur, Belgium)</p> <p>Country: Belgium</p> <p>Dates: 7-25 November 2020</p> <p>Symptoms and severity: 118, 63% symptomatic</p> <p>Demographics: women (n = 104, 55%): median age 54 years (range 5-97 years) Men (n = 84): median age 57 years (range 1-94 years)</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: [A] Biotical SARS-CoV-2 Ag card [B] Panbio COVID-19 Ag Rapid Test Device [C] Coronavirus Ag Rapid Test Cassette [D] Roche SARS-CoV-2 Rapid Antigen Test (Additional lab-based Ag test also evaluated but not eligible for this review: [E] VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test (Ortho Clinical Diagnostics, Raritan, NJ, USA))</p> <p>Manufacturer: [A] Biotical Health, Madrid, Spain [B] Abbott, Chicago, IL, USA [C] Healgen Scientific, Houston, TX, USA [D] Roche Diagnostics, Basel, Switzerland</p> <p>Antibody: [A] to [D] Nucleocapsid</p> <p>Ag target: not stated</p> <p>Test method: [A] to [D] all LFAs, method not reported [E] Chemiluminescence assay</p> <p>Samples used: NP in VTM; collection not described</p> <p>Transport media: ESwab liquid preservation medium (Copan Italia, Brescia, Italy) or Vacuette Virus Stabilization (Greiner Bio-One, Kremsmünster, Austria) tubes</p> <p>Sample storage: all tests performed within 24 h of collection; storage conditions not described</p> <p>Test operator: laboratory staff</p>

Favresse 2021 [A] (Continued)

Definition of test positivity: appearance of 2 visible lines for all except VITRO which was a signal of ≥ 1

Blinding reported: yes, 2 independent operators with a 3rd blinded operator in case of disagreement. All operators were blinded to PCR results and clinical data

Timing of samples: symptomatic: median 3 days pso (IQR 2-4 days)

Target condition and reference standard(s)

Reference standard: PCR; LightCycler (Roche Diagnostics, Basel, Switzerland) 480 Instrument II (Roche Diagnostics) using the LightMix (Roche Diagnostics) Modular SARS-CoV E-gene set; Ct threshold appears to be ≤ 38 (range in Ct values reported was 12.6-38.2)

Definition of non-COVID cases: unclear but appears single negative PCR for absence of infection

Genetic target(s): E-gene

Samples used: same sample as for index test

Timing of reference standard: same as index

Blinded to index test: unclear; "All tests were performed within a maximum of 24 h after specimen collection", but order of tests was not reported

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same sample

All participants received same reference standard: yes

Missing data: none mentioned

Uninterpretable results: none mentioned

Indeterminate results (index test): none mentioned

Indeterminate results (reference standard): none mentioned

Comparative

Notes

Funding: no external funding

Publication status: published paper

Source: academic journal

Author COI: among the authors, JD is CEO and founder of QUALIblood s.a., a contract research organization manufacturing the DP-Filter, is co-inventor of the DP-Filter (patent application number: PCT/ET2019/052903) and reports personal fees from Daiichi-Sankyo, Gedeon Richter, Mithra Pharmaceuticals, Stago, Roche and Roche Diagnostics outside the submitted work. The other authors have no conflict of interest to disclose.

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Unclear		
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Was a case-control design avoided?	Yes		
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Favresse 2021 [A] *(Continued)*

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Favresse 2021 [A] *(Continued)*

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Favresse 2021 [B]
Study characteristics

Patient Sampling Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Index tests Comparative study of 5 Ag tests (no product codes reported); Favresse 2021 [B] relates to test [B] in the list below; see Favresse 2021 [A] for full study characteristics and QUADAS entries

Test name: [A] Biotical SARS-CoV-2 Ag card
[B] Panbio COVID-19 Ag Rapid Test Device
 [C] Coronavirus Ag Rapid Test Cassette
 [D] Roche SARS-CoV-2 Rapid Antigen Test
 (Additional lab-based Ag test also evaluated but not eligible for this review: [E] VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test (Ortho Clinical Diagnostics, Raritan, NJ, USA))

Manufacturer: [A] Biotical Health, Madrid, Spain
[B] Abbott, Chicago, IL, USA
 [C] Healgen Scientific, Houston, TX, USA
 [D] Roche Diagnostics, Basel, Switzerland

Antibody: **[A] to [D] Nucleocapsid**

Ag target: not stated

Test method: **[A] to [D] all LFAs, method not reported**
 [E] Chemiluminescence assay

Samples used: NP in VTM; collection not described

Transport media: ESwab liquid preservation medium (Copan Italia, Brescia, Italy) or Vacuette Virus Stabilization (Greiner Bio-One, Kremsmünster, Austria) tubes

Sample storage: all tests performed within 24 h of collection; storage conditions not described

Test operator: laboratory staff

Definition of test positivity: appearance of 2 visible lines for all except VITRO which was a signal of ≥ 1

Blinding reported: yes, 2 independent operators with a 3rd blinded operator in case of disagreement. All operators were blinded to PCR results and clinical data

Timing of samples: symptomatic: median 3 days pso (IQR 2-4 days)

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Favresse 2021 [B] (Continued)

Target condition and reference standard(s) Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Flow and timing Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Comparative

Notes

Favresse 2021 [C]

Study characteristics

Patient Sampling Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Index tests Comparative study of 5 Ag tests (no product codes reported); Favresse 2021 [C] relates to test [C] in the list below; see Favresse 2021 [A] for full study characteristics and QUADAS entries

Test name: [A] Biotical SARS-CoV-2 Ag card

[B] Panbio COVID-19 Ag Rapid Test Device

[C] Coronavirus Ag Rapid Test Cassette

[D] Roche SARS-CoV-2 Rapid Antigen Test

(Additional lab-based Ag test also evaluated but not eligible for this review: [E] VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test (Ortho Clinical Diagnostics, Raritan, NJ, USA))

Manufacturer: [A] Biotical Health, Madrid, Spain

[B] Abbott, Chicago, IL, USA

[C] Healgen Scientific, Houston, TX, USA

[D] Roche Diagnostics, Basel, Switzerland

Antibody: **[A] to [D] Nucleocapsid**

Ag target: not stated

Test method: **[A] to [D] all LFAs, method not reported**

[E] Chemiluminescence assay

Samples used: NP in VTM; collection not described

Transport media: ESwab liquid preservation medium (Copan Italia, Brescia, Italy) or Vacuette Virus Stabilization (Greiner Bio-One, Kremsmünster, Austria) tubes

Sample storage: all tests performed within 24 h of collection; storage conditions not described

Test operator: laboratory staff

Definition of test positivity: appearance of 2 visible lines for all except VITRO which was a signal of ≥ 1

Blinding reported: yes, 2 independent operators with a 3rd blinded operator in case of disagreement. All operators were blinded to PCR results and clinical data

Timing of samples: symptomatic: median 3 days pso (IQR 2-4 days)

Favresse 2021 [C] (Continued)

Target condition and reference standard(s) Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Flow and timing Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Comparative

Notes

Favresse 2021 [D]
Study characteristics

Patient Sampling Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Index tests Comparative study of 5 Ag tests (no product codes reported); Favresse 2021 [D] relates to test [D] in the list below; see Favresse 2021 [A] for full study characteristics and QUADAS entries

Test name: [A] Biotical SARS-CoV-2 Ag card

[B] Panbio COVID-19 Ag Rapid Test Device

[C] Coronavirus Ag Rapid Test Cassette

[D] Roche SARS-CoV-2 Rapid Antigen Test

(Additional lab-based Ag test also evaluated but not eligible for this review: [E] VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test (Ortho Clinical Diagnostics, Raritan, NJ, USA))

Manufacturer: [A] Biotical Health, Madrid, Spain

[B] Abbott, Chicago, IL, USA

[C] Healgen Scientific, Houston, TX, USA

[D] Roche Diagnostics, Basel, Switzerland

Antibody: **[A] to [D] Nucleocapsid**

Ag target: not stated

Test method: **[A] to [D] all LFAs, method not reported**

[E] Chemiluminescence assay

Samples used: NP in VTM; collection not described

Transport media: eSwab liquid preservation medium (Copan Italia, Brescia, Italy) or Vacuette Virus Stabilization (Greiner Bio-One, Kremsmünster, Austria) tubes

Sample storage: all tests performed within 24 h of collection; storage conditions not described

Test operator: laboratory staff

Definition of test positivity: appearance of 2 visible lines for all except VITRO which was a signal of ≥ 1

Blinding reported: yes, 2 independent operators with a 3rd blinded operator in case of disagreement. All operators were blinded to PCR results and clinical data

Timing of samples: symptomatic: median 3 days pso (IQR 2-4 days)

Favresse 2021 [D] (Continued)

Target condition and reference standard(s) Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Flow and timing Comparative study of 5 Ag tests; Favresse 2021 [A] reports full study characteristics and QUADAS.

Comparative

Notes

Fenollar 2020(a)

Study characteristics

Patient Sampling 2 cohorts of patients presenting for COVID-19 testing at the same institution. This extraction relates to:
[1] single-group study to estimate sensitivity alone: symptomatic patients, all PCR positive (n = 182)
Fenollar 2020(b) reports data for [2] single-group study to estimate both sensitivity and specificity: asymptomatic contacts of confirmed cases (n = 159)

Recruitment: prospective

Prospective or retrospective: unclear

Patient characteristics and setting Setting: unclear; COVID-19 testing

Location: Institut Hospitalo-universitaire Méditerranée Infection, Marseille

Country: France

Dates: 21 September-2 October 2020

Symptoms and severity: not stated; all symptomatic
Ct values for 154 participants: Ct ≤ 20: 58, 38%; Ct 21-25: 49, 32%; Ct 26-30: 39, 25%; Ct 31-34: 8, 5%

Demographics: not reported

Exposure history: [1] not stated

Index tests Test name: Panbio COVID-19 Ag

Manufacturer: Abbott

Antibody: NP

Ag target: not stated

Test method: not stated

Samples used: NP

Transport media: not stated; appears to be direct testing

Sample storage: tested within 1 h

Test operator: not stated

Definition of test positivity: visual line; as per manufacturer IFU

Fenollar 2020(a) (Continued)

	Blinding reported: not stated, but presume yes as conducted within 1 h of collection Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: automated RT-PCR; VitaPCR (Credo diagnostics, Singapore) Definition of non-COVID cases: n/a Genetic target(s): not stated Samples used: NP (paired, from opposite nostril) Timing of reference standard: not stated Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swabs All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported, no participant flow diagram reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "supported by the Méditerranée-Infection Foundation and the French Agence Nationale de la Recherche under reference Investissements d'Avenir Méditerranée Infection 10-IAHU-03 and Région Provence-Alpes-Côte d'Azur and European funding FEDER IHUBIOTK." Source: accepted manuscript Author COI: "Pr Raoult and Pr Drancourt are co-founders of the Pocrame startup that develops diagnostic devices for infectious diseases"

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 inclusions?	Unclear		
Could the selection of patients have introduced bias?		High risk	

Fenollar 2020(a) *(Continued)*

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Fenollar 2020(b)
Study characteristics

Patient Sampling	<p>2 cohorts of patients presenting for COVID-19 testing at the same institution. This extraction relates to: [2] single-group study to estimate both sensitivity and specificity: asymptomatic contacts of confirmed cases (n = 159) See Fenollar 2020(a) for extraction of additional cohort: [1] single-group study to estimate sensitivity alone: symptomatic patients, all PCR positive (n = 182)</p> <p>Recruitment: prospective</p> <p>Prospective or retrospective: unclear</p>
Patient characteristics and setting	<p>Setting: unclear</p> <p>Location: Institut Hospitalo-universitaire Méditerranée Infection, Marseille</p> <p>Country: France</p> <p>Dates: 21 September-2 October 2020</p> <p>Symptoms and severity: all asymptomatic; 21/22 cases had Ct > 25</p> <p>Demographics: not reported</p> <p>Exposure history: [2] all described as contacts</p>
Index tests	<p>Test name: PANBIO COVID-19 Ag</p> <p>Manufacturer: Abbott</p> <p>Antibody: NP</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP</p> <p>Transport media: not stated; appears to be direct testing</p> <p>Sample storage: tested within 1 h</p> <p>Test operator: not stated</p> <p>Definition of test positivity: visual line; as per manufacturer IFU</p> <p>Blinding reported: not stated, conducted first</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: automated RT-PCR; VitaPCR (Credo diagnostics, Singapore)</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP (paired, from opposite nostril)</p> <p>Timing of reference standard: not stated</p> <p>Blinded to index test: unclear</p>

Fenollar 2020(b) (Continued)

	Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swabs All participants received same reference standard: yes Missing data: none reported, no participant flow diagram reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "supported by the Méditerranée-Infection Foundation and the French Agence Nationale de la Recherche under reference Investissements d'Avenir Méditerranée Infection 10-IAHU-03 and Région Provence-Alpes-Côte d'Azur and European funding FEDER IHUBIOTK." Source: accepted manuscript Author COI: "Pr Raoult and Pr Drancourt are co-founders of the Pocrame startup that develops diagnostic devices for infectious diseases"

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Fenollar 2020(b) *(Continued)*

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Ferguson 2021
Study characteristics

Patient Sampling	Single-group study estimating sensitivity and specificity: university students attending asymptomatic student testing centre at the University of Birmingham Recruitment: consecutive inclusion of LFD-positive samples; random sample of LFD-negative (confirmatory PCR for 90 samples/d of testing) Prospective or retrospective: prospective Sample size (cases): 720 (8)
Patient characteristics and setting	Setting: mass screening Location: University of Birmingham

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Ferguson 2021 (Continued)

Country: UK
 Dates: 2-9 December 2020
 Symptoms and severity: all asymptomatic
 Demographics: not stated
 Exposure history: not stated

Index tests

Test name: Innova Lateral Flow Device
 Manufacturer: Innova Medical group, a subsidiary of Xiamen Biotime Biotechnology company
 Antibody: SARS-CoV-2 nucleocapsid antigens
 Ag target: not stated
 Test method: CGIA
 Samples used: NP; supervised self-collection
 States NP but process described involves swabbing both tonsils (so OP) and 1 nasal cavity = nasal+OP?
 Transport media: none used; immediately processed according to the Innova protocol
 Sample storage: no storage
 Test operator: not stated
 Trained postgraduate and final year undergraduate students in the College of Medical and Dental Science, supervised by highly experienced postdoctoral researchers (total of 18 test operatives)
 Definition of test positivity: not stated; visual appearance of lines
 Blinding reported: yes; conducted first
 Timing of samples: N/A; all asymptomatic, no clear epidemiological contact reported

Target condition and reference standard(s)

Reference standard: PCR; ThermoFisher Covid-19 taqPath assay
 Positivity threshold: 2 of 3 gene targets amplifying at a Ct value of ≤ 35
 Definition of non-COVID cases: as for cases; single negative
 Genetic target(s): not stated
 ORF1ab, N gene, S gene (Table 2)
 Samples used: residual NP swabs
 Timing of reference standard: same as for index test
 Blinded to index test: not stated
 Yes; "All samples were completely anonymous to the testing team with no identifying labels and were arbitrarily numbered from 1 to 90 each day"
 Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous; paired swab; same swab "residual LFD test samples (buffer solution in which the NP swab is resuspended to perform the test)"
 All participants received same reference standard: yes
 Missing data: yes

Ferguson 2021 (Continued)

Uninterpretable results: none
 4 invalid on Ag test; "Results of 4 samples were void (as defined by the manufacturer's protocol [2])"

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: "the PCR testing in this manuscript is funded by the UK Department for Health and Social Care (DHSC) as part of pillar 2 testing, in an award made directly to the University of Birmingham. The provision of LFD tests is funded by DHSC as part of a national student testing program, and funded directly to the University of Birmingham. DHSC have had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript."

Publication status: published

Source: PLOS Biology

Author COI: no competing interests exist.

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Ferguson 2021 (Continued)

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Filgueiras 2021
Study characteristics

Patient Sampling Single-group study estimating sensitivity and specificity: patients with clinical features and suspected COVID-19 seen by ED doctors; later described as "hospitalised"

Recruitment: not clear; all who were tested before admission

Prospective or retrospective: not stated; appears prospective

Filgueiras 2021 (Continued)

Sample size (cases): 150 (55)

Patient characteristics and setting	<p>Setting: inpatient; patients at the ED prior to admission to hospital</p> <p>Location: reference hospital in Belo Horizonte</p> <p>Country: Brazil</p> <p>Dates: June-August 2020</p> <p>Symptoms and severity: all symptomatic: 72 (48.0%) dyspnoea, 52 (34.7%) dry cough, 50 (33.3%) fever, 49 (32.7%) myalgia, 25 (16.7%) asthenia and 24 (16.0%) productive cough 127 (84.7%) had ≥ 2 associated symptoms; 15 (10%) had 5-7 associated symptoms Of PCR+, 36 (65.5%) critically ill; 19/19 with typical findings of patchy ground-glass shadows on CT presented bilateral pneumonia, compared to 5/11 (45.5%) of COVID-19-negative individuals with same alteration</p> <p>Demographics: median age 62 years (range 29-91 years), 22 (40.0%) male</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: COVID-19 Ag ECO Test</p> <p>Manufacturer: ECODiagnostica, Brazil</p> <p>Ag target: Nucleocapsid</p> <p>Test method: CGIA</p> <p>Samples used: NP swabs</p> <p>Transport media: not stated; appears that none used</p> <p>Sample storage: immediately tested</p> <p>Test operator: not stated</p> <p>Definition of test positivity: colorimetric reaction; interpreted after a 15-min incubation</p> <p>Blinding reported: not stated, but very likely considering test was done prior to reference standard</p> <p>Timing of samples: at 1st day of symptom onset ≤ 3 days 63 (42%); 4-7 days 59 (39%); 8-15 days 22 (15%); > 15 days 2 (1%), not reported 4 (3%)</p>
Target condition and reference standard(s)	<p>Reference standard: PCR; Allplex 2019-nCov Assay kit (Seegene Inc., Republic of Korea) IFU states PCR inconclusive if only 1 or 2 of 3 targets detected (Ct < 40); re-test recommended</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): Gene E, Gene RdRP and Gene N MS2</p> <p>Samples used: NP swabs (paired); pre-processed samples stored under refrigeration until RNA extraction</p> <p>Timing of reference standard: same as for index</p> <p>Blinded to index test: not stated; performed by the Minas Gerais Reference Center for the Diagnosis of COVID-19</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous; paired swab</p>

Filgueiras 2021 (Continued)

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none

Indeterminate results (reference standard): none

11 samples with inconclusive results (only 1 Ag+ve); 5 on day 1 or 2 pso, 2 on day 5, 1 on day 8, 1 on day 15; and not reported for 2 samples

2/11 had bilateral multifocal ground-glass opacities on CT, and 4 needed oxygen supply due to strong dyspnoea and desaturation; 1 (Ag positive) with odynophagia and dry cough. Not clear whether all were considered to have COVID-19

Unit of analysis: participant

Comparative

Notes

Funding: "Oswaldo Cruz Foundation (to RFQG and scholarships to CC, RA, LC, NC), The Brazilian National Council for Scientific and Technological Development (CNPq) (scholarships to AO, DM, SG), Coordination for the Improvement of Higher Education Personnel (CAPES) (scholarships to NA, JA), The Minas Gerais Research Funding Foundation (FAPEMIG) (scholarship to PF). EcoDiagnostica for attending our request for donation of diagnostic kits under evaluation."

Publication status: published

Source: medRxiv

Author COI: no COI statement

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		

Filgueiras 2021 (Continued)

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

FIND 2020a

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: patients with symptoms consistent with COVID-19 (meeting national definition for testing) presenting at a community testing clinic</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: community (COVID-19 testing clinic)</p> <p>Location: institution not described; Marica, Rio de Janeiro</p> <p>Country: Brazil</p> <p>Dates: 30 July-21 August 2020</p> <p>Symptoms and severity: all symptomatic; no further details</p> <p>Demographics: mean age 40 years (range 4-84); reported for 396 participants 181 (45%) male</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: NowCheck COVID-19 Ag test (RG1901DG)</p> <p>Manufacturer: Bionote Inc</p> <p>Antibody: SARS-CoV-2 nucleocapsid antigen</p> <p>Ag target: mouse monoclonal SARS-CoV-2 antibodies</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: proprietary NP swab collected by HCW</p> <p>Transport media: no transport media. Sample is immediately transferred to proprietary tube containing extraction buffer.</p> <p>Sample storage: test should be performed as soon as possible after collection. Specimens may be stored at room temperature for 1 h or 2-8 °C for 4 h.</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 4 days pso (IQR 3-6 days); day < 0-3, 152, 39% day 4-7, 180, 46% day ≥ 8, 58, 15%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR (in-house assay based on the US CDC protocol); Ct threshold of 37</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): N1, N2</p> <p>Samples used: NP swabs</p>

FIND 2020a (Continued)

	Timing of reference standard: same timing as per NP swabs for index test
	Blinded to index test: yes
	Incorporated index test: no
Flow and timing	Time interval between index and reference tests: 0 to several days based on PCR turnaround times at the lab
	All participants received same reference standard: yes
	Missing data: reports 0 invalid results
	Uninterpretable results: none
	Indeterminate results (index test): none reported
	Indeterminate results (reference standard): none reported
	Unit of analysis: participant
Comparative	
Notes	Funding: FIND
	Publication status: published
	Source: FIND website/IFU index test
	Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020a (Continued)

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2020b (CH)
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity at 2 sites. This extraction is for data from Switzerland (see FIND 2020b (DE) for extraction of data for German site): patients seeking COVID-19 testing at main testing centre; described as presenting either with symptoms compatible with a SARS-CoV-2 infection, or with a known positive contact or asymptomatic HCWs (n = 535)</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	Setting: community (main testing centre)

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020b (CH) (Continued)

	<p>Location: Hopitaux Universitaires de Geneve (HUG), Geneva</p> <p>Country: Switzerland</p> <p>Dates: 9-16 October 2020</p> <p>Symptoms and severity: 534/535 symptomatic (99%)</p> <p>Demographics: mean age 38.5 years (16-85 years) 247, 46% male</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Panbio Covid-19 Ag Rapid Test (41FK10)</p> <p>Manufacturer: Abbott</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: CGIA (from product insert)</p> <p>Samples used: NP</p> <p>Transport media: no transport media; assay buffer used</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: time pso recorded for 115/124, 92%. Day 0-3 89, 78%; day 4-7 23, 20%; day 8+ 3, 3%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR Roche Cobas; Ct threshold < 40 (from Figure)</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP swab (paired, from contralateral nostril)</p> <p>Timing of reference standard: not stated; author contact advises only paired swabs used</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: reports 0 invalid</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p>

FIND 2020b (CH) (Continued)

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: FIND

Publication status: published

Source: FIND/HUG website/IFU index test

Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020b (CH) (Continued)

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2020b (DE)
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity at 2 sites; this extraction is for data from Germany (see [FIND 2020b \(CH\)](#) for data related to the site in Switzerland). Some information extracted from preprint reporting the same evaluations (see secondary reference under [FIND 2020b \(DE\)](#) for 2020 preprint by Kruger and colleagues): patients seeking COVID-19 testing at main testing centre; described as presenting either with symptoms compatible with a SARS-CoV2 infection, or with a known positive contact or asymptomatic HCWs (n = 1108)

Recruitment: consecutive recruitment

Prospective or retrospective: prospective

Sample size (cases): 1108 (106)

Patient characteristics and setting Setting: COVID-19 test centre

Location: [1] Heidelberg drive-in testing; [2] Berlin: ambulatory testing clinic of Charité – University Hospital

Country: Germany

Dates: [1] Heidelberg: 28 September-30 October 2020; [2] Berlin: 19 October-30 October 2020

Symptoms and severity: 709/1100 symptomatic (64.5%). 2020 preprint by Kruger and colleagues reports 712 (65%) with symptoms on the day of testing (mean symptom duration 4.01 ± 3.1 (n = 687)); 396 (35%) with no symptoms

Demographics: mean age 38.7 years (18-86 years), 542, 49% male; 367 (33%) with comorbidities (see secondary reference under [FIND 2020b \(DE\)](#) for 2020 preprint by Kruger and colleagues)

FIND 2020b (DE) (Continued)

Exposure history: 388/858 (45.2%) Heidelberg participants were tested based on high risk contacts without symptoms (see secondary reference under [FIND 2020b \(DE\)](#) for 2020 preprint by Kruger and colleagues)

Index tests

Test name: Panbio Covid-19 Ag (41FK10)

Manufacturer: Abbott Rapid Diagnostics

Antibody: not reported

Ag target: not reported

Test method: CGIA (from product insert)

Samples used: NP or OP (if NP was contradicted) collected by trained study team; also referred to as laboratory personnel

Transport media: no transport media; assay buffer used

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: trained laboratory team

Definition of test positivity: presence of visible control and test lines

Blinding reported: yes

Timing of samples: time pso recorded for 692/709 symptomatic, 98%

Day 0-3 380, 55%

Day 4-7 230, 33%

Day 8+ 82, 12%

Target condition and reference standard(s)

Reference standard: PCR; one of 5 assays:

1. Cobas SARS-CoV-2 (Roche Diagnostics Inc); n = 236
2. Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) n = 45
3. Allplex 2019-nCov Assay (Seegene Inc); n = 725
4. LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); n = 15
5. Cobas (Roche) or Thermofisher (Multiplex TaqPath COVID-19 CE-IVD PCR Kit); n = 88

Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs

Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection

Genetic target(s): not stated

Samples used: NP swab (paired, from contralateral nostril)

Timing of reference standard: as for index test; paired swabs used

Blinded to index test: yes

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab

All participants received same reference standard: yes

Missing data: none reported; no invalid tests (0%). 2020 preprint by Kruger and colleagues reports 10 withdrew consent for second swab and 1 had invalid PCR

FIND 2020b (DE) (Continued)

Uninterpretable results: not reported; invalid test results were repeated once with the remaining buffer solution in the test tubes.

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: FIND

Publication status: published

Source: FIND report

Author COI: none stated (these are independent evaluations)

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Yes		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate inclusions?	Yes		
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Could the selection of patients have introduced bias?		Low risk	
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Are there concerns that the included patients and setting do not match the review question?			Low concern
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DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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If a threshold was used, was it pre-specified?	Yes		
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Could the conduct or interpretation of the index test have introduced bias?		Low risk	
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Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020b (DE) (Continued)

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2020c (BR)
Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity at 3 sites; this extraction is for data from Brazil (see FIND 2020c (CH) and FIND 2020c (DE) for extraction of data from other sites): ambulatory patients meeting national suspect definition for COVID-19 testing presenting at a community testing clinic in Brazil
	Recruitment: consecutive recruitment
	Prospective or retrospective: prospective

FIND 2020c (BR) (Continued)

<p>Patient characteristics and setting</p>	<p>Setting: community testing clinic</p> <p>Location: Macae, state of Rio de Janeiro</p> <p>Country: Brazil</p> <p>Dates: 13-30 July 2020</p> <p>Symptoms and severity: 392/397 (99%) symptomatic; no further details</p> <p>Demographics: mean age 37 years (2-94); 397 participants; 229/398 male (57%)</p> <p>Exposure history: not stated</p>
<p>Index tests</p>	<p>Test name: STANDARD Q COVID-19 Ag (09COV30D)</p> <p>Manufacturer: SD Biosensor Inc</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: NP; collected by HCW</p> <p>Transport media: proprietary swab/media provided by SD Biosensor</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 5 days pso (IQR 4-6 days) (for 397 participants); day < 0-3 85, 21%; day 4-7, 273, 69%; day ≥ 8, 39, 10%</p>
<p>Target condition and reference standard(s)</p>	<p>Reference standard: RT-PCR (In-house; Lab-developed assay based on the US CDC protocol; Ct threshold not stated; author contact advises Ct thresholds as per assay IFUs</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): N1 and N2</p> <p>Samples used: NP swabs</p> <p>Timing of reference standard: not stated; author contact advises only paired swabs used</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
<p>Flow and timing</p>	<p>Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: reports 0 missing data</p>

FIND 2020c (BR) (Continued)

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: FIND

Publication status: published

Source: FIND website/IFU index test

Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020c (BR) *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

FIND 2020c (CH)
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity at single site; this extraction is for data from Switzerland (see FIND 2020c (BR) and FIND 2020c (DE) for extraction of data from other sites): patients seeking COVID-19 testing at main testing centre; described as presenting either with symptoms compatible with a SARS-CoV2 infection, or with a known positive contact or asymptomatic HCWs (n = 529; from total cohort of 1064 volunteers)</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: community (main testing centre)</p> <p>Location: Hopitaux Universitaires de Geneve (HUG), Geneva</p> <p>Country: Switzerland</p> <p>Dates: 9-23 October 2020</p> <p>Symptoms and severity: not stated; time pso recorded for 183/191, 96% 141/183 COVID positive cases had symptoms for 0-4 days (77%)</p> <p>Demographics: not stated</p>

FIND 2020c (CH) (Continued)

	Exposure history: not stated
Index tests	<p>Test name: STANDARD Q COVID-19 Ag (09COV30D)</p> <p>Manufacturer: SD Biosensor Inc</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: NP</p> <p>Transport media: proprietary swab/media provided by SD Biosensor</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median not reported (range 0-15); day < 0-3, 122, 67%; day 4-7, 54, 29%; day 8+; 7, 34%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR Roche Cobas; Ct threshold < 40 (from Figure)</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP swab (paired, from contralateral nostril)</p> <p>Timing of reference standard: not stated; author contact advises only paired swabs used</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: reports 0 missing data</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: FIND</p> <p>Publication status: published</p>

FIND 2020c (CH) (Continued)

Source: FIND/HUG websites/IFU index test

Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

FIND 2020c (CH) (Continued)

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Low risk

FIND 2020c (DE)
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity at 3 sites; this extraction is for data from Germany (see [FIND 2020c \(BR\)](#) and [FIND 2020c \(CH\)](#) for extraction of data from the other 2 sites evaluating this assay). Some information extracted from preprint reporting the same evaluations (see secondary reference under [FIND 2020c \(DE\)](#) for 2020 preprint by Kruger and colleagues): patients at risk for SARS-CoV-2 infection based on exposure to a confirmed case, suggestive symptoms, or travel to a high-risk area, presenting either at a drive-in testing station or a clinical ambulatory testing facility

Recruitment: Consecutive, as per FIND evaluation protocol

Prospective or retrospective: prospective

Patient characteristics and setting

Setting: COVID-19 testing centres

Location: (1) Heidelberg, Germany; (2) Berlin, Germany

Country: Germany

Dates: (1) Heidelberg: 20-31 July 2020 (2) Berlin: 03 June -31 July 2020

Participants undergoing assay (b)

Symptomatic on testing day: 10 40/1229, 84.6%

Mean age (range): 35 (18-80.4) based on 1244 participants

Male (%): 606, 49.5%

Exposure history: not stated

Index tests

Test name: STANDARD Q COVID-19 Ag Test

Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea

Antibody: not stated

Ag target: not stated

FIND 2020c (DE) (Continued)

Test method: CGIA

Samples used: Heidelberg NP; Berlin combined NP and OP (OP conducted first)
RT-PCR swab obtained first, then same technique repeated for Ag test

Transport media: none; used manufacturer supplied buffer solution as per IFU

Sample storage: drive-in centre and ambulatory testing: tested on site (presume short time frame)
Secondary care: transported on ice to a category 3 facility for testing
RT-PCR swab obtained first, then same technique repeated for Ag test

Test operator: drive-in and ambulatory clinic: POC evaluation
Secondary care: laboratory staff

Definition of test positivity: visual appearance were interpreted by 2 operators, each blinded to the result of the other. In case of discrepant results, both operators re-read the result and agreed on a final result.

Invalid results were repeated once using the remaining buffer according to the respective IFUs.
Readouts were done within the recommended time for each Ag-RDT (10 min for Bioeasy, 15 min for Coris and 15-30 min for SD Biosensor).

Blinding reported: yes; "Staff performing the Ag-RDTs were blinded to results of RT-PCR tests and vice versa"

Timing of samples: mean 3 days pso (IQR 2-4 days) based on 1004 participants

Target condition and reference standard(s)

Reference standard: RT-PCR; varied by site

1. Cobas SARS-CoV-2 (Roche Diagnostics Inc) ; n = 912 (Berlin)
2. Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) ; n = 78 (Heidelberg)
3. Allplex 2019-nCov Assay (Seegene Inc) ; n = 125 (Heidelberg)

Samples that showed a signal above the threshold in the relevant RT-PCR target regions for each assay were considered to be positive

Definition of non-COVID cases: as per cases; single negative result

Genetic target(s): not stated

Samples used: paired swabs; as per index test (RT-PCR swab obtained first)
Drive-in centre: NP or OP
Other centres: combined NOP (OP conducted first)

Timing of reference standard: as per index test

Blinded to index test: yes; "Staff performing the Ag-RDTs were blinded to results of RT-PCR tests and vice versa"

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired; simultaneous

All participants received same reference standard: yes (different assays)

Missing data: 2020 preprint by Kruger and colleagues reports total of 154 excluded from German sites (3 assays evaluated) following enrolment (116 2nd swab refused, 3 nose bleed after 1st swab, 3 insufficient time for both swabs, 31 other reasons, 1 no reason available)

Uninterpretable results: 0 invalid reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

FIND 2020c (DE) (Continued)

Unit of analysis: participant

Comparative

Notes

Funding: study was supported by FIND, Heidelberg University Hospital and Charité – University Hospital internal funds.

Publication status: published

Source: FIND report

Author COI: no COI statement reported; "external funders of the study had no role in study design, data collection, or data analysis"

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020c (DE) (Continued)

Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Low risk

FIND 2020d (BR)
Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity at 2 sites; this extraction is for data from Brazil (see FIND 2020d (DE) for extraction of data from other site): adults in community meeting national suspect definition for COVID-19 testing presenting at [1] a community testing clinic or [2] a tertiary-level hospital Recruitment: consecutive recruitment Prospective or retrospective: prospective
Patient characteristics and setting	Setting: mixed; community testing clinic and tertiary hospital

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020d (BR) (Continued)

Location: [1] Macae, state of Rio de Janeiro, [2] Universidade Federal do Rio de Janeiro (UFRJ)

Country: Brazil

Dates: [1] 17 August-9 September, [2] 11 July-8 August 2020

Symptoms and severity: 421/450 (94%) symptomatic; no further details

Demographics: mean age 39 years (0-95 years); 451 participants; 185 male (41%)

Exposure history: not stated

Index tests

Test name: STANDARD F COVID-19 Ag FIA (F-NCOV-01G, 10COV30D)

Manufacturer: SD Biosensor Inc

Antibody: not reported

Ag target: not reported

Test method: FIA

Samples used: NP; collected by HCW

Transport media: proprietary swab/media provided by SD Biosensor

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: HCW

Definition of test positivity: as per STANDARD F Analyzer; cut-off index (COI) ≥ 1.0 (as per IFU)

Blinding reported: yes

Timing of samples: median 4 days pso (IQR 3-6 days) for 421 participants. Day < 0-3, 131, 31%; day 4-7, 248, 59%; day ≥ 8 , 42, 10%

Target condition and reference standard(s)

Reference standard: RT-PCR; 1 of 2 in-house assays:

1. lab-developed assay based on the US CDC protocol
2. lab-developed assay based on the Charité Universitätsmedizin Berlin protocol

Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs

Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection

Genetic target(s):

1. N1 and N2
2. E and RdRp

Samples used: NP swabs

Timing of reference standard: not stated; author contact advises only paired swabs used

Blinded to index test: yes

Incorporated index test: no

FIND 2020d (BR) (Continued)

Flow and timing

Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab

All participants received same reference standard: yes

Missing data: reports 0 missing data

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: FIND

Publication status: published

Source: FIND website/IFU for index test

Author COI: none stated (these are independent evaluations)

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Yes		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate inclusions?	Yes		
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Could the selection of patients have introduced bias?		Low risk	
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Are there concerns that the included patients and setting do not match the review question?			Low concern
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DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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If a threshold was used, was it pre-specified?	Yes		
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Could the conduct or interpretation of the index test have introduced bias?		Low risk	
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FIND 2020d (BR) (Continued)

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

Low concern

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2020d (DE)
Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity at 2 sites; this extraction is for data from Germany (see FIND 2020d (BR) for extraction of data from other site); adults in community meeting national suspect definition for COVID-19 testing presenting at [1] a drive-in testing centre or [2] ambulatory testing clinic Recruitment: consecutive recruitment Prospective or retrospective: prospective
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020d (DE) (Continued)

Patient characteristics and setting	<p>Setting: community</p> <p>Location: [1] Heidelberg, drive-in testing; [2] Berlin, ambulatory testing clinic of Charité University Hospital</p> <p>Country: Germany</p> <p>Dates: [1] Heidelberg: 15 June-18 July 2020; [2] Berlin: 6 July-23 September 2020</p> <p>Symptoms and severity: 517/669 (77%) symptomatic; no further details</p> <p>Demographics: mean age 38 years (18-85 years); 676 participants; 307 male (46%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: STANDARD F COVID-19 Ag FIA (F-NCOV-01G, 10COV30D)</p> <p>Manufacturer: SD Biosensor Inc</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: FIA</p> <p>Samples used: [1] NP; [2] combined NOP swabs; collected by HCW</p> <p>Transport media: proprietary swab/media provided by SD Biosensor</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: as per STANDARD F Analyzer; cut-off index (COI) ≥ 1.0 (as per IFU)</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 3 days pso (IQR 2-5 days) for 505 participants. Day < 0-3, 257, 51%; day 4-7, 202, 47%; day ≥ 8, 46, 9%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; one of 5 assays:</p> <ol style="list-style-type: none"> 1. Cobas SARS-CoV-2 (Roche Diagnostics Inc); n = 342 2. Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) n = 1 3. Allplex 2019-nCov Assay (Seegene Inc); n = 20 4. LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); n = 233 5. Cobas (Roche) or ThermoFisher (Multiplex TaqPath COVID-19 CE-IVD RT-PCR Kit); n = 80 <p>Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): not stated apart from 3. E gene</p> <p>Samples used: NP (n = 305), NOP (n = 342) and/or OP swabs (n = 32)</p> <p>Timing of reference standard: not stated; author contact advises only paired swabs used</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>

FIND 2020d (DE) (Continued)

Flow and timing	Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab All participants received same reference standard: yes Missing data: reports 0 missing data Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
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Comparative

Notes	Funding: FIND Publication status: published Source: FIND website/IFU for index test Author COI: none stated (these are independent evaluations)
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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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

FIND 2020d (DE) (Continued)

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

Low concern

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2020e (BR)
Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity; this extraction is for data from Brazil (see FIND 2020e (DE) for extraction of data from other site): adults in community meeting national suspect definition for COVID-19 testing presenting at a community testing clinic (n = 476) Recruitment: consecutive recruitment Prospective or retrospective: prospective
Patient characteristics and setting	Setting: community testing clinic

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020e (BR) (Continued)

	<p>Location: Marica, state of Rio de Janeiro</p> <p>Country: Brazil</p> <p>Dates: 27 July-16 September 2020</p> <p>Symptoms and severity: 470/476 (99%) symptomatic; no further details</p> <p>Demographics: mean age 45 years (0-106 years); 473 participants; 252 male (53%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: BIOCREDIT COVID-19 Ag (G61RHA20 - product evaluated is no longer distributed)</p> <p>Manufacturer: RapiGEN Inc</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: LFA (CGIA, from IFU)</p> <p>Samples used: NP; collected by HCW</p> <p>Transport media: assay diluent provided by manufacturer</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: visual appearance of test and control lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 5 days pso (IQR 4-7 days) for 470 participants. Day < 0-3, 95, 20%; day 4-7, 296, 63%; day ≥ 8, 79, 17%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; lab-developed assay based on the US CDC protocol Ct threshold not stated; author contact advises Ct thresholds as per assay IFUs</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): N1 and N2</p> <p>Samples used: NP swabs</p> <p>Timing of reference standard: not stated; author contact advises only paired swabs used</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: reports 0 missing data</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020e (BR) (Continued)

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: FIND

Publication status: published

Source: FIND website/IFU for index test

Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020e (BR) (Continued)

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2020e (DE)
Study characteristics

Patient Sampling

Single-group study to estimate sensitivity and specificity at 2 sites; this extraction is for data from Germany (see [FIND 2020e \(BR\)](#) for extraction of data from other site): adults in community meeting national suspect definition for COVID-19 testing presenting at [1] a drive-in testing centre or [2] ambulatory testing clinic

Recruitment: consecutive recruitment

Prospective or retrospective: prospective

Patient characteristics and setting

Setting: community

Location: [1] Heidelberg, drive-in testing; [2] Berlin, ambulatory testing clinic of Charité University Hospital

Country: Germany

Dates: [1] Heidelberg: 4 May-3 September; [2] Berlin: 4 May-18 August

Symptoms and severity: 733/1223 symptomatic; no further details

Demographics: mean age 39.5 years (17-59.2 years) 1239 participants); 607 male (50%)

Exposure history: not stated

Index tests

Test name: BIOCREDIT COVID-19 Ag (G61RHA20 - product evaluated is no longer distributed)

Manufacturer: RapiGEN Inc

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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FIND 2020e (DE) (Continued)

Antibody: not reported

Ag target: not reported

Test method: LFA (CGIA, from IFU)

Samples used: [1] NP; [2] NOP; collected by HCW

Transport media: assay diluent provided by manufacturer

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: HCW

Definition of test positivity: visual appearance of test and control lines

Blinding reported: yes

Timing of samples: median 3 days pso (IQR 2-4days) for 701 participants. Day < 0-3, 472, 67%; day 4-7, 161, 23%; day ≥ 8, 68, 10%

Target condition and reference standard(s) Reference standard: RT-PCR; one of 5 assays:

1. Cobas SARS-CoV-2 (Roche Diagnostics Inc); n = 344
2. Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) n = 114
3. Allplex 2019-nCov Assay (Seegene Inc); n = 571
4. LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); n = 132
5. RealStar SARS-CoV-2 RT-PCR Kit (Altona Diagnostics); n = 80

Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs

Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection

Genetic target(s): not stated

Samples used: NP swabs

Timing of reference standard: not stated; author contact advises only paired swabs used

Blinded to index test: yes

Incorporated index test: no

Flow and timing Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab

All participants received same reference standard: yes

Missing data: reports 0 missing data

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: FIND

FIND 2020e (DE) (Continued)

Publication status: published

Source: FIND website/IFU for index test

Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		

FIND 2020e (DE) (Continued)

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Low risk

FIND 2020f
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity (other assays evaluated at the same sites in Germany are included as FIND 2021j and FIND 2020c (DE)). Some information extracted from 2020 preprint by Kruger and colleagues reporting the same evaluations (see secondary reference under FIND 2020f).</p> <p>Participants at risk for SARS-CoV-2 infection based on exposure to a confirmed case, suggestive symptoms, or travel to a high-risk area, presenting either at (1) a drive-in testing station or (2) a clinical ambulatory testing facility ("adults able to ambulate and meeting suspect definition of the Department of public health")</p> <p>(3) secondary care facility in the UK (adults admitted and suspected to have COVID-19 with following symptoms: fever $\geq 37.8^{\circ}\text{C}$ +/- shortness of breath +/- new persistent cough +/- loss of smell OR clinical or radiological evidence of pneumonia)</p> <p>Recruitment: consecutive, as per FIND evaluation protocol</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: mixed; COVID-19 testing centres and secondary care</p> <p>Location: 3 sites: (1) Heidelberg, Germany; (2) Berlin, Germany and (3) Liverpool University Hospital Foundation Trust, Liverpool</p> <p>Country: (1), (2) Germany, (3) UK</p> <p>Dates: (1) HD: 11-25 May; (2) Berlin: 10 Aug; 19-25 Aug; (3) Liverpool: 12 May-19 June</p> <p>Symptomatic on testing day: 290/419, 69.2%</p> <p>N with prior negative test result: 38/301, 12.6%</p> <p>Mean age (IQR): 43 years (18, 89 years)</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020f (Continued)

Male (%): 163/418, 39%

Index tests	<p>Test name: COVID-19 Ag Respi-Strip</p> <p>Manufacturer: Coris Bioconcept, Gembloux, Belgium Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: drive-in centre: NP, Other centres: combined NOP (OP conducted first) RT-PCR swab obtained first, then same technique repeated for Ag test</p> <p>Transport media: none; used manufacturer supplied buffer solution as per IFU</p> <p>Sample storage: drive-in centre and ambulatory testing: tested on site (presume short time frame) Secondary care: transported on ice to a category 3 facility for testing RT-PCR swab obtained first, then same technique repeated for Ag test</p> <p>Test operator: drive-in and ambulatory clinic: POC evaluation Secondary care: laboratory staff</p> <p>Definition of test positivity: visual appearance interpreted by 2 operators, each blinded to the result of the other. In case of discrepant results, both operators re-read the result and agreed on a final result. Invalid results were repeated once using the remaining buffer according to the respective IFUs. Readouts were done within the recommended time for each Ag-RDT (15 min for Coris)</p> <p>Blinding reported: yes; "Staff performing the Ag-RDTs were blinded to results of RT-PCR tests and vice versa"</p> <p>Timing of samples: 3 days (IQR 1-5 days); based on 282 participants</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; varied by site</p> <ol style="list-style-type: none"> Allplex 2019-nCov Assay (Seegene Inc); Heidelberg Cobas SARS-CoV-2 (Roche Diagnostics Inc); Berlin Genesig COVID-19 Real-Time PCR Assay (Primerdesign, Ltd.); UK LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); Heidelberg, Berlin Abbott (Illinois, US) RealTime 2019-nCoV assay; Heidelberg <p>Samples that showed a signal above the threshold in the relevant RT-PCR target regions for each assay were considered to be positive</p> <p>Definition of non-COVID cases: as per cases; single negative result</p> <p>Genetic target(s): not stated</p> <p>Samples used: paired swabs, combined NOP; as per index test (RT-PCR swab obtained first)</p> <p>Timing of reference standard: as per index test</p> <p>Blinded to index test: yes; "Staff performing the Ag-RDTs were blinded to results of RT-PCR tests and vice versa"</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired; simultaneous</p> <p>All participants received same reference standard: yes (different assays)</p> <p>Missing data: 2020 preprint by Kruger and colleagues (FIND 2020f) reports total of 154 excluded from German sites (3 assays evaluated) following enrolment (116 2nd swab refused, 3 nose bleed after 1st swab, 3 insufficient time for both swabs, 31 other reasons, 1 no reason available)</p>

FIND 2020f (Continued)

Uninterpretable results: 8 invalid (PCR negative)

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Study reports an ease-of-use assessment; for this assay:

- challenges due to inconsistent test result interpretation (often only very faint lines visible) and deficiencies in both the test kit quality and design

Funding: study was supported by FIND, Heidelberg University Hospital and Charité – University Hospital internal funds. Pfizer funded the clinical team in Liverpool, UK

Publication status: preprint

Source: medRxiv

Author COI: no COI statement reported; "external funders of the study had no role in study design, data collection, or data analysis"

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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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 inclusions?

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?

High

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?

Yes

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

Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2020f (Continued)

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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

High risk

FIND 2021a [A]
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: patients with symptoms consistent with COVID-19 (meeting national definition for testing) presenting at a community testing clinic</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 218 (79)</p>
Patient characteristics and setting	<p>Setting: community (COVID-19 testing clinic)</p> <p>Location: institution not described; Marica and Guapimirim, state of Rio de Janeiro</p> <p>Country: Brazil</p> <p>Dates: 21-27 January 2021; 23-26 February 2021</p> <p>Symptoms and severity: all symptomatic; no further details</p> <p>Demographics: mean age 42.3 years (range 18-90); 92 (42%) male</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: [A] NowCheck COVID-19 Ag test (RG1901DGN (Nasal)) [B] NowCheck COVID-19 Ag test (RG1901DG (NP))</p> <p>Manufacturer: Bionote Inc</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: [A] NMT [B] NP swab collected by HCW</p> <p>Transport media: no transport media. Sample is immediately transferred to proprietary tube containing extraction buffer.</p> <p>Sample storage: immediate testing</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 4 days pso (IQR 3-6 days); day < 0-3, 72, 33% day 4 -7, 123, 56% day ≥ 8, 23, 11%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR (in-house assay based on the US CDC protocol); Ct threshold of 37</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): N1, N2</p>

FIND 2021a [A] (Continued)

	Samples used: NP swabs
	Timing of reference standard: same timing as for index test
	Blinded to index test: yes
	Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous, paired swabs
	All participants received same reference standard: yes
	Missing data: reports 0 invalid results for both assays
	Uninterpretable results: none reported
	Indeterminate results (index test): none reported
	Indeterminate results (reference standard): none reported
	Unit of analysis: participant
Comparative	
Notes	Funding: FIND
	Publication status: published
	Source: FIND website/IFU index test
	Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		

FIND 2021a [A] (Continued)

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 (Evaluations of serial (repeat) testing)	
DOMAIN 3: Reference Standard	
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

FIND 2021a [B]

Study characteristics	
Patient Sampling	Comparative study of an Ag test on 2 different samples; FIND 2021a [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of an Ag test on 2 different samples; FIND 2021a [A] reports full study characteristics and QUADAS.
Index tests	Test name: [A] NowCheck COVID-19 Ag test (RG1901DGN (Nasal)) [B] NowCheck COVID-19 Ag test (RG1901DG (NP))

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2021a [B] *(Continued)*

Manufacturer: Bionote Inc

Antibody: not reported

Ag target: not reported

Test method: rapid chromatographic immunoassay in lateral flow format

Samples used: [A] NMT

[B] NP swab

collected by HCW

Transport media: no transport media. Sample is immediately transferred to proprietary tube containing extraction buffer.

Sample storage: immediate testing

Test operator: HCW

Definition of test positivity: presence of visible control and test lines

Blinding reported: yes

Timing of samples: median 4 days pso (IQR 3-6 days);

day < 0-3, 72, 33%

day 4-7, 123, 56%

day ≥ 8, 23, 11%

Target condition and reference standard(s)	Comparative study of an Ag test on 2 different samples; FIND 2021a [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of an Ag test on 2 different samples; FIND 2021a [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of an Ag test on 2 different samples; FIND 2021a [A] reports full study characteristics and QUADAS.

FIND 2021b [A]
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity at single site: patients seeking COVID-19 testing at COVID-19 testing centre; described as able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting suspect definition of the Department of Public Health (n = 281)</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 281 (44)</p>
Patient characteristics and setting	<p>Setting: community</p> <p>Location: Heidelberg drive-in testing</p> <p>Country: Germany</p>

FIND 2021b [A] (Continued)

Dates: 15 December 2020-19 January 2021

Symptoms and severity: 130/279 symptomatic (46%)

Demographics: mean age 42.9 years (range 18-81 years)
134, 48% male

Exposure history: not stated

Index tests

Test name: **[A] Panbio™ Covid-19 Ag Rapid Test Device Nasal (41FK11)**
[B] Panbio COVID-19 Ag Rapid Test (41FK10)

Manufacturer: Abbott

Antibody: not reported

Ag target: not reported

Test method: CGIA (from product insert)

Samples used: **[A] NMT**
[B] NP

Transport media: no transport media; assay buffer used

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: HCW

Definition of test positivity: presence of visible control and test lines

Blinding reported: yes

Timing of samples: time pso recorded for 126/281, 45%
Day 0-3 86, 68%
Day 4-7 290, 23%
Day 8+ 11, 9%

Target condition and reference standard(s)

Reference standard: RT-PCR; one of 3 assays:

1. Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) n = 3
2. Allplex 2019-nCov Assay (Seegene Inc); n = 13
3. LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); n = 266

Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs

Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection

Genetic target(s): not stated

Samples used: NP swab

Timing of reference standard: not stated; author contact advises only paired swabs used.

Blinded to index test: yes

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired swabs; 0 to several days based on PCR turnaround times at the lab

All participants received same reference standard: yes

FIND 2021b [A] (Continued)

Missing data: none reported; 0 invalid results

Uninterpretable results: none

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: FIND

Publication status: published

Source: FIND website/IFU for index test

Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			

FIND 2021b [A] (Continued)

Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

FIND 2021b [B]
Study characteristics

Patient Sampling	Comparative study of an Ag test on 2 different samples; FIND 2021b [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	
Index tests	Test name: [A] Panbio™ Covid-19 Ag Rapid Test Device Nasal (41FK11) [B] Panbio COVID-19 Ag Rapid Test (41FK10) Manufacturer: Abbott Antibody: not reported Ag target: not reported Test method: CGIA (from product insert) Samples used: [A] NMT [B] NP

FIND 2021b [B] (Continued)

Transport media: no transport media; assay buffer used

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: HCW

Definition of test positivity: presence of visible control and test lines

Blinding reported: yes

Timing of samples: time pso recorded for 126/281, 45%

Day 0-3, 86, 68%

Day 4-7, 290, 23%

Day 8+, 11, 9%

Target condition and reference standard(s)	Comparative study of an Ag test on 2 different samples; FIND 2021b [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of an Ag test on 2 different samples; FIND 2021b [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of an Ag test on 2 different samples; FIND 2021b [A] reports full study characteristics and QUADAS.

FIND 2021c (BR) [A]

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity at 2 sites; (see FIND 2021c (DE) [A] for additional site data): ambulatory patients meeting national suspect definition for COVID-19 testing presenting at a community testing clinic in Brazil</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 214 (78)</p>
Patient characteristics and setting	<p>Setting: community testing clinic</p> <p>Location: Macae and Guapimirim, state of Rio de Janeiro</p> <p>Country: Brazil</p> <p>Dates: 14-20 January 2021; 2-4 March 2021</p> <p>Symptoms and severity: all symptomatic; no further details</p> <p>Demographics: mean age 41.3 years (range 18-77 years) ; 85/214 male (40%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: [A] STANDARD Q COVID-19 Ag Nasal (09COV31D) [B] STANDARD Q COVID-19 Ag (09COV30D)</p> <p>Manufacturer: SD Biosensor Inc</p>

FIND 2021c (BR) [A] (Continued)

	<p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: [A] NTM [B] NP; collected by HCW</p> <p>Transport media: proprietary swab/media provided by SD Biosensor</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 5 days pso (IQR 3-6.75 days); day < 0-3, 68, 32% day 4-7, 116, 54% day ≥ 8, 30, 14%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR (in-house; lab-developed assay based on the US CDC protocol; Ct threshold not stated; author contact advises Ct thresholds as per assay IFUs</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): N1 and N2</p> <p>Samples used: NP swabs</p> <p>Timing of reference standard: not stated; author contact advises only paired swabs used</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swabs</p> <p>All participants received same reference standard: yes</p> <p>Missing data: reports 0 missing data; 0 invalid results</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: FIND</p> <p>Publication status: published</p> <p>Source: FIND website/IFU index test</p>

FIND 2021c (BR) [A] (Continued)

Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High

FIND 2021c (BR) [A] *(Continued)*
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

FIND 2021c (BR) [B]
Study characteristics

Patient Sampling	Comparative study of an Ag test on 2 different samples; FIND 2021c (BR) [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of an Ag test on 2 different samples; FIND 2021c (BR) [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] STANDARD Q COVID-19 Ag Nasal (09COV31D) [B] STANDARD Q COVID-19 Ag (09COV30D)</p> <p>Manufacturer: SD Biosensor Inc</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: [A] NTM [B] NP collected by HCW</p> <p>Transport media: proprietary swab/media provided by SD Biosensor</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 5 days pso (IQR 3-6.75 days): day < 0-3, 68, 32% day 4-7, 116, 54% day ≥ 8, 30, 14%</p>

FIND 2021c (BR) [B] *(Continued)*

Target condition and reference standard(s)	Comparative study of an Ag test on 2 different samples; FIND 2021c (BR) [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of an Ag test on 2 different samples; FIND 2021c (BR) [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of an Ag test on 2 different samples; FIND 2021c (BR) [A] reports full study characteristics and QUADAS.

FIND 2021c (DE) [A]
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity at 2 sites; (see FIND 2021c (BR) [A] for additional site data): 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</p> <p>Recruitment: consecutive recruitment; continued until 30 positive NP swab samples according to Ag-RDT were obtained</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 179 (41)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre</p> <p>Location: ambulatory testing clinic of Charité – University Hospital</p> <p>Country: Germany</p> <p>Dates: 11-18 November 2020</p> <p>Symptoms and severity: on day of testing: 172 (96%) symptomatic; 7 (4%) asymptomatic; average symptom duration 4.2 ± 2.6 days</p> <p>Demographics: average age 36.2 ± 12.2 years; 48% female; 14% with comorbidities</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: [A] STANDARD Q COVID-19 Ag Nasal (09COV31D) [B] STANDARD Q COVID-19 Ag (09COV30D)</p> <p>Manufacturer: SD Biosensor Inc</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: [A] NMT (both sides of nose); [B] NP (single side of nose); Both HCW collected; states 'professional' (secondary paper for FIND 2021c (DE) [A] by Lindner and colleagues describes study physicians collecting swabs).</p> <p>Transport media: proprietary swab/media provided by SD Biosensor</p>

FIND 2021c (DE) [A] (Continued)

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: HCW

Definition of test positivity: presence of visible control and test lines

Blinding reported: yes

Timing of samples: median 4 days pso (IQR 3-5 days) for 397 patients:

day < 0-3, 79, 46%

day 4-7, 76, 44%

day ≥ 8, 18, 10%

Target condition and reference standard(s)

Reference standard: PCR; 1. Cobas SARS-CoV-2 (Roche Diagnostics Inc); n = 158. 2. LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol) n = 21
 Ct threshold not stated; author contact advises Ct thresholds as per assay IFUs

Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection

Genetic target(s): not stated

Samples used: NP/OP swab; opposite nostril

Timing of reference standard: not stated; author contact advises only paired swabs used

Blinded to index test: yes

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired swabs

All participants received same reference standard: yes

Missing data: 1 patient was excluded as both swabs for the Ag could not be obtained

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative
Notes

Funding: FIND

Publication status: published

Source: FIND website/IFU index test

Author COI: none stated (these are independent evaluations)

Methodological quality
Item
Authors' judgement
Risk of bias
Applicability concerns
DOMAIN 1: Patient Selection

FIND 2021c (DE) [A] *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	

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FIND 2021c (DE) [A] (Continued)

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2021c (DE) [B]
Study characteristics

Patient Sampling Comparative study of 2 versions of an Ag test; [FIND 2021c \(DE\) \[A\]](#) details full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 2 versions of an Ag test; [FIND 2021c \(DE\) \[A\]](#) details full study characteristics and QUADAS.

Index tests Test name: [A] STANDARD Q COVID-19 Ag Nasal (09COV31D)
[B] STANDARD Q COVID-19 Ag (09COV30D)

Manufacturer: SD Biosensor Inc

Antibody: not reported

Ag target: not reported

Test method: rapid chromatographic immunoassay in lateral flow format

Samples used: [A] AN
[B] NP
 collected by HCW

Transport media: proprietary swab/media provided by SD Biosensor

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: HCW

Definition of test positivity: presence of visible control and test lines

Blinding reported: yes

Timing of samples: median 4 days pso (IQR 3-5 days) for 397 participants:
 day < 0-3, 79, 46%
 day 4-7, 76, 44%
 day ≥ 8, 18, 10%

Target condition and reference standard(s) Comparative study of 2 versions of an Ag test; [FIND 2021c \(DE\) \[A\]](#) details full study characteristics and QUADAS.

Flow and timing Comparative study of 2 versions of an Ag test; [FIND 2021c \(DE\) \[A\]](#) details full study characteristics and QUADAS.

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2021c (DE) [B] *(Continued)*

Comparative

Notes	Comparative study of 2 versions of an Ag test; FIND 2021c (DE) [A] details full study characteristics and QUADAS.
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FIND 2021d
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: 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 and presenting at [1] a drive-in testing centre or [2] ambulatory testing clinic</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 214 (78)</p>
Patient characteristics and setting	<p>Setting: community</p> <p>Location: [1] Heidelberg drive in testing; [2] Berlin: ambulatory testing clinic of Charité – University Hospital</p> <p>Country: Germany</p> <p>Dates: [1] Heidelberg: 20 January–19 February 2021; [2] Berlin: 18 January–22 February 2021</p> <p>Symptoms and severity: symptomatic 62% (446/718); no further details</p> <p>Demographics: mean age 39.4 years (range 18–80 years); 348/719 male (48%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Espline SARS-CoV-2 (231906)</p> <p>Manufacturer: Fujirebio Inc.</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: NP (OP only if NP contraindicated); collected by HCW using iAMP-COV-ID19-SCD</p> <p>Transport media: none</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 2 days pso (IQR 1–4 days):</p>

FIND 2021d (Continued)

day < 0-3, 311, 70%
 day 4-7, 106, 24%
 day ≥ 8, 27, 6%

Target condition and reference standard(s)	<p>Reference standard: RT-PCR; one of 3 assays:</p> <ol style="list-style-type: none"> 1. Cobas SARS-CoV-2 (Roche Diagnostics Inc); n = 299 2. Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) n = 1 3. LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); n = 423 <p>Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): only stated for 3. (E-gene)</p> <p>Samples used: NP swabs (or OP if used for Ag test)</p> <p>Timing of reference standard: not stated; author contact advises only paired swabs used</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swabs</p> <p>All participants received same reference standard: yes</p> <p>Missing data: reports 0 missing data; 0 invalid results</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: FIND</p> <p>Publication status: published</p> <p>Source: FIND website/IFU index test</p> <p>Author COI: none stated (these are independent evaluations)</p>

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		

FIND 2021d (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2021d (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2021e
Study characteristics

Patient Sampling

Single-group study to estimate sensitivity and specificity: adults in community meeting Department of Public Health definition of a suspected COVID-19 case and being tested for SARS-CoV-2 part of routine medical care

Recruitment: consecutive recruitment

Prospective or retrospective: prospective

Sample size (cases): 265 (44)

Patient characteristics and setting

Setting: COVID-19 test centre

Location: Hopitaux Universitaires de Geneve (HUG), Geneva

Country: Switzerland

Dates: 4-13 January 2021

Symptoms and severity: only reported for PCR+ group; symptomatic 88.6% (39/44)

Demographics: mean age 36.3 years (range 16-80 years); 139/265 male (52%)

Exposure history: not stated

Index tests

Test name: SARS-CoV-2 Antigen Rapid Test Kit (Colloidal Gold) (COV-AG-20/G10313)

Manufacturer: Joysbio (Tianjin) Biotechnology Co

Antibody: not reported

Ag target: not reported

Test method: rapid chromatographic immunoassay in lateral flow format

Samples used: AN; collected by HCW

Transport media: none

Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU

Test operator: HCW

Definition of test positivity: presence of visible control and test lines

Blinding reported: yes

Timing of samples: only reported for PCR+ cases, median 2 days pso (IQR 1-3.5 days):
 day < 0-3, 23, 74%
 day 4-7, 8, 26%

FIND 2021e (Continued)

day ≥ 8, 0, 0%

Target condition and reference standard(s)	Reference standard: RT-PCR; one of 3 assays: <ol style="list-style-type: none"> 1. Cobas SARS-CoV-2 (Roche Diagnostics Inc); (n = 216) 2. Xpert Xpress SARS-CoV-2 (Cepheid) (n = 1) 3. TaqPath COVID-19 CE IVD RT PCR Kit (Thermo Fisher Scientific) (with Nimbus Presto Extraction instrument) (n = 48) <p>Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP swabs</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swabs</p> <p>All participants received same reference standard: yes</p> <p>Missing data: reports 0 missing data; 0 invalid results</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: FIND</p> <p>Publication status: published</p> <p>Source: FIND website/IFU index test</p> <p>Author COI: none stated (these are independent evaluations)</p>

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 inclusions?	Yes		

FIND 2021e (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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Low risk

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2021f
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: 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, presenting either at:</p> <ol style="list-style-type: none"> 1. Heidelberg: drive-in testing centre 2. Berlin: ambulatory testing clinic <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 665 (194)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre</p> <p>Location: 1. Heidelberg: drive-in testing centre; 2. Berlin: ambulatory testing clinic of Charité – University Hospital</p> <p>Country: Germany</p> <p>Dates: 1. Heidelberg: 11-31 March 2021; 2. Berlin: 11 March–15 April 2021</p> <p>Symptoms and severity: symptomatic: 66.5%, (440/662)</p> <p>Demographics: mean age 38.7 years (range 18-78 years); 331/664 male (50%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: COVID 19 RAPID ANTIGEN TEST (11811125)</p> <p>Manufacturer: Mologic Ltd</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: nasal (AN) (n = 645) or NMT (n = 20); collected by HCW</p> <p>Transport media: none</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: median 2 days pso (IQR 1-4 days); n = 436 day < 0-3, 290, 67% day 4-7, 121, 28% day ≥ 8, 25, 6%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; one of 2 assays:</p> <ol style="list-style-type: none"> 1. LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); n = 323 2. Cobas SARS-CoV-2 (Roche Diagnostics Inc); n = 342

FIND 2021f (Continued)

Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs

Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection

Genetic target(s): not stated

Samples used: HD: NP swabs (oropharyngeal if NP contraindicated)
 Berlin: combined NP/oropharyngeal swabs

Timing of reference standard: as for index test

Blinded to index test: yes

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired swabs

All participants received same reference standard: yes

Missing data: yes

Uninterpretable results: 16/665, 2.4% invalid Ag results (including 3 PCR+ and 13 PCR-samples)

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative
Notes

Funding: FIND

Publication status: published

Source: FIND website/IFU index test

Author COI: none stated (these are independent evaluations)

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 inclusions?	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

FIND 2021f (Continued)

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2021g
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: individuals (age 16+) in community meeting Department of Public Health definition of a suspected COVID-19 case and being tested for SARS-CoV-2 part of routine medical care</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 462 (69)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre</p> <p>Location: University Hospital of Geneva</p> <p>Country: Switzerland</p> <p>Dates: 24 November 2020-20 January 2021</p> <p>Symptoms and severity: reported for PCR+ only; symptomatic 94.2% (65/69)</p> <p>Demographics: mean age 38.7 years (range 16-82 years); 206/462 male (45%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: COVID-19 Ag Rapid Test (243103N-20)</p> <p>Manufacturer: NADAL</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: NP swab; collected by HCW</p> <p>Transport media: none</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: only reported for 54/62 PCR+ patients Median 2 days pso (IQR 1-3 days) day < 0-3, 45, 83% day 4-7, 7, 13% day ≥ 8, 2, 4%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; one of 3 assays:</p> <ol style="list-style-type: none"> 1. Cobas SARS-CoV-2 (Roche Diagnostics Inc) (n = 217) 2. Cobas SARS-CoV-2 & Influenza A/B (Roche Diagnostics Inc) (n = 72) 3. TaqPath COVID-19 CE IVD RT PCR Kit (Thermo Fisher Scientific) (with Nimbus Presto Extraction instrument) (n = 173) <p>Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs</p>

FIND 2021g (Continued)

	Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection Genetic target(s): not stated Samples used: NP swab Timing of reference standard: as for index test Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: paired swabs All participants received same reference standard: yes Missing data: none; reports 0 invalid Uninterpretable results: none Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: FIND Publication status: published Source: FIND website/IFU index test Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			

FIND 2021g (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2021h
Study characteristics

FIND 2021h (Continued)

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: individuals (age 16+) in community meeting Department of Public Health definition of a suspected COVID-19 case and being tested for SARS-CoV-2 part of routine medical care</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 232 (41)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre</p> <p>Location: University Hospital of Geneva</p> <p>Country: Switzerland</p> <p>Dates: 21-29 January 2021</p> <p>Symptoms and severity: reported for PCR+ only; symptomatic 92.7% (38/41)</p> <p>Demographics: mean age 36.3 years (range 16-76 years); 103/232 male (44%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: iChroma COVID-19 Ag Test (CFPC-115)</p> <p>Manufacturer: Boditech Medical, Inc.</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: rapid chromatographic immunoassay in lateral flow format</p> <p>Samples used: NP swab; collected by HCW</p> <p>Transport media: none</p> <p>Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU</p> <p>Test operator: HCW</p> <p>Definition of test positivity: presence of visible control and test lines</p> <p>Blinding reported: yes</p> <p>Timing of samples: only reported for 32 PCR+ patients Median 1.5 days pso (IQR 1-3 days) day < 0-3, 26, 81% day 4-7, 5, 16% day ≥ 8, 1, 3%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; one of 2 assays:</p> <ol style="list-style-type: none"> 1. Cobas SARS-CoV-2 (Roche Diagnostics Inc) (n = 35) 2. Cobas SARS-CoV-2 & Influenza A/B (Roche Diagnostics Inc) (n = 197) <p>Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs</p> <p>Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection</p> <p>Genetic target(s): not stated</p>

FIND 2021h (Continued)

	Samples used: NP swab
	Timing of reference standard: as for index test
	Blinded to index test: yes
	Incorporated index test: no
Flow and timing	Time interval between index and reference tests: paired swabs
	All participants received same reference standard: yes
	Missing data: none; reports 0 invalid
	Uninterpretable results: none
	Indeterminate results (index test): none reported
	Indeterminate results (reference standard): none reported
	Unit of analysis: participant
Comparative	
Notes	Funding: FIND
	Publication status: published
	Source: FIND website/IFU index test
	Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		

FIND 2021h (Continued)

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 (Evaluations of serial (repeat) testing)	
DOMAIN 3: Reference Standard	
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

FIND 2021i
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: individuals (age 16+) in community meeting Department of Public Health definition of a suspected COVID-19 case and being tested for SARS-CoV-2 part of routine medical care</p> <p>Recruitment: consecutive recruitment</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 328 (56)</p>
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

FIND 2021i (Continued)

Patient characteristics and setting	Setting: COVID-19 test centre Location: University Hospital of Geneva Country: Switzerland Dates: 3-11 December 2020 Symptoms and severity: reported for PCR+ only; symptomatic 100% (56/56) Demographics: mean age 37.9 years (range 16-76 years); 129/327 male (39%) Exposure history: not stated
Index tests	Test name: Wondfo 2019-nCoV Antigen Test (W196P0003) Manufacturer: Guangzhou Wondfo Biotech Co. Antibody: not reported Ag target: not reported Test method: rapid chromatographic immunoassay in lateral flow format Samples used: NP swab; collected by HCW Transport media: none Sample storage: author contact advises tested as soon as possible and within the time limit specified in the IFU Test operator: HCW Definition of test positivity: presence of visible control and test lines Blinding reported: yes Timing of samples: only reported for 44 PCR+ patients Median 2 days pso (IQR 1-4 days) day < 0-3, 31, 70% day 4-7, 11, 25% day ≥ 8, 2, 5%
Target condition and reference standard(s)	Reference standard: RT-PCR; one of 3 assays: <ol style="list-style-type: none"> 1. Cobas SARS-CoV-2 (Roche Diagnostics Inc) (n = 137) 2. Xpert Xpress SARS-CoV-2 (Cepheid) (n = 1) 3. TaqPath COVID-19 CE IVD RT PCR Kit (Thermo Fisher Scientific) (with Nimbus Presto Extraction instrument) (n = 192) Ct thresholds not stated; author contact advises Ct thresholds as per assay IFUs Definition of non-COVID cases: same as for cases. Single negative PCR required for absence of infection Genetic target(s): not stated Samples used: NP swab Timing of reference standard: as for index test Blinded to index test: yes Incorporated index test: no

FIND 2021i (Continued)

Flow and timing	Time interval between index and reference tests: paired swabs
	All participants received same reference standard: yes
	Missing data: none; reports 0 invalid
	Uninterpretable results: none
	Indeterminate results (index test): none reported
	Indeterminate results (reference standard): none reported
	Unit of analysis: participant

Comparative

Notes	Funding: FIND
	Publication status: published
	Source: FIND website/IFU index test
	Author COI: none stated (these are independent evaluations)

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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

FIND 2021i (Continued)

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

FIND 2021j
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity (other assays evaluated at the same sites in Germany are included as [FIND 2020f](#) and [FIND 2020c \(DE\)](#)). Some information extracted from 2020 preprint by Kruger and colleagues reporting the same evaluations (see secondary reference under [FIND 2021j](#)).

Participants at risk for SARS-CoV-2 infection based on exposure to a confirmed case, suggestive symptoms, or travel to a high-risk area, presenting either at (1) a drive-in testing station or (2) a clinical ambulatory testing facility ("adults able to ambulate and meeting suspect definition of the Department of public health")

Recruitment: not stated; recorded as consecutive, as per FIND evaluation protocol

Prospective or retrospective: prospective

Sample size (cases): 729 (15)

FIND 2021j (Continued)

Patient characteristics and setting	Setting: mixed; (1), (2) Community (drive-in or clinical ambulatory testing) Location: 2 sites: (1) Heidelberg, Germany; (2) Berlin, Germany Country: (1), (2) Germany Dates: (1) 14 April-3 May 2020; (2) 14 May-3 Jun 2020 Symptomatic on testing day: 563/654, 86.1% Mean age (SD): 40 (18.1-92.0); n = 728 Male (%): 47.2% (369/699)
Index tests	Test name: Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit (Time-Resolved Fluorescence) Manufacturer: Shenzhen Bioeasy Biotechnology Co. Ltd., Guangdong Province, China Antibody: not stated Ag target: not stated Test method: FIA Samples used: (1) NP (or OP if NP contraindicated); (2) combined NOP (OP conducted first) PCR swab obtained first, then same technique repeated for Ag test Transport media: none; used manufacturer supplied buffer solution as per IFU (for the Bioeasy assay, "the developer requested for pipettes to be used to transfer adequate quantities of liquid; in the IFU no pipette is needed and a nozzle is provided"). Sample storage: tested on site (presume short time frame) PCR swab obtained first, then same technique repeated for Ag test. Test operator: drive-in and ambulatory clinic: POC evaluation Definition of test positivity: as per Analyzer Invalid results were repeated once using the remaining buffer according to the respective IFUs. Readouts were done within the recommended time: 10 min for Bioeasy Blinding reported: yes; "Staff performing the Ag-RDTs were blinded to results of PCR tests and vice versa" Timing of samples: median 3 days pso (IQR 2-6 days); n = 540; < 3 days, 303 (56%), 4-7 days, 132 (24%), day 8+, 105 (19%)
Target condition and reference standard(s)	Reference standard: PCR; varied by site <ol style="list-style-type: none"> Cobas SARS-CoV-2 (Roche Diagnostics Inc); n = 223 Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc); n = 5 Allplex 2019-nCov Assay (Seegene Inc); n = 343 LightMix Modular SARS-CoV (COVID19) E-gene (Tib Molbiol); n = 158 Samples that showed a signal above the threshold in the relevant PCR target regions for each assay were considered to be positive Definition of non-COVID cases: as per cases; single negative result Genetic target(s): not stated Samples used: paired swabs; as per index test (PCR swab obtained first); (1) NP or OP, (2) combined NOP (OP conducted first) Timing of reference standard: as per index test

FIND 2021j (Continued)

Blinded to index test: yes; "Staff performing the Ag-RDTs were blinded to results of PCR tests and vice versa"

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired; simultaneous

All participants received same reference standard: yes (different assays)

Missing data: Yes uninterpretable excluded

Uninterpretable results: 2 invalid excluded

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative
Notes

Study reports an ease-of-use assessment; for this assay:

- a high number of test execution steps (including precision pipetting)... challenges when performing multiple tests at the same time possibly hindering the test's wide-spread use

Funding: study was supported by FIND, Heidelberg University Hospital and Charité – University Hospital internal funds.

Publication status: Published

Source: FIND report

Author COI: no COI statement reported; "external funders of the study had no role in study design, data collection, or data analysis"

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 inclusions?	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 (Evaluations of single test application)			

FIND 2021j (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

FIND 2021j (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Fourati 2020 [A]
Study characteristics

Patient Sampling	<p>2-group study to estimate sensitivity and specificity:</p> <ol style="list-style-type: none"> 1. residual samples from patients with positive SARS-CoV-2 PCR tested when they presented symptoms at the time of the first epidemic wave (n = 297) 2. pre-pandemic samples (n = 337) <p>Recruitment: random (stratified by Ct and time pso)</p> <p>Prospective or retrospective: retrospective</p>
Patient characteristics and setting	<p>Setting: mixed; likely outpatient and inpatient "consulted or were admitted"</p> <p>Location: Henri Hospital Mondor de Créteil</p> <p>Country: France</p> <p>Dates: 9 March-9 April 2020</p> <p>Symptoms and severity: not stated; all apparently symptomatic</p> <p>Data by viral load reported for 293/297 cases: ≤ 20 Ct 39, 13%; 2-25 Ct 88, 30%; 25-30 Ct 72, 25%; > 30 Ct 88, 30%</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] data relate to test [A], see additional entries for tests [B] to [E]</p> <p>[A] SARS-CoV-2 COVID-19 Respi-Strip [B] STANDARD Q COVID-19 Ag [C] PanBio COVID-19 Antigen Rapid Test [D] Biosynex COVID-19 Ag BSS [E] COVID-VIRO Antigen Rapid Test [F] NG Test SARS-CoV-2 Ag (assay excluded from review due to Vortex requirement as stated in IFU) (no product codes reported)</p> <p>Manufacturer:</p> <p>[A] Coris BioConcept, Gembloux, Belgium [B] SD BIOSENSOR, Inc., Korea [C] Abbott, Chicago, Illinois, USA [D] Biosynex, Strasbourg, France [E] AAZ, Boulogne-Billancourt, France [F] NG Biotech, Guipry, France</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p>

Fourati 2020 [A] (Continued)

	<p>Test method: not stated</p> <p>Samples used: NP; collection not reported</p> <p>Transport media: VTM (Cepheid or Deltalab); 100 µL used for testing</p> <p>Sample storage: frozen at -80 °C until use</p> <p>Test operator: laboratory staff</p> <p>Definition of test positivity: visual, as per manufacturer IFU</p> <p>Blinding reported: yes; each test was interpreted independently by 2 different laboratory technicians. A 3rd reading was carried out in the event of discrepancy</p> <p>Timing of samples: pso (reported for 289 samples): 0-3 days 97, 34%; 4-7 days 103, 36%; 8-11 days 63, 22%; ≥ 12 days 26, 9%</p> <p>Number of samples reported at > 7 days varied per test, maximum was 289</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; in-house assay developed by CNR (Institut Pasteur) or RealStar SARS-CoV-2 (Altona Diagnostics, Germany)</p> <p>Definition of non-COVID cases: pre-pandemic</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP; same as for index</p> <p>Timing of reference standard: as for index</p> <p>Blinded to index test: yes, seems to be at time of sampling</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same swab; simultaneous</p> <p>All participants received same reference standard: yes</p> <p>Missing data: number of cases missing per assay varied; reasons for missing data not reported (presumably invalid assay results)</p> <p>[A] 5, 1.7%</p> <p>[B] 6, 2.0%</p> <p>[C] 2, 0.7%</p> <p>[D] 0</p> <p>[E] 2, 0.7%</p> <p>[F] 0</p> <p>Uninterpretable results: not stated</p> <p>Indeterminate results (index test): not stated</p> <p>Indeterminate results (reference standard): not stated</p> <p>Unit of analysis: presume patients</p>
Comparative	
Notes	<p>Funding: evaluation of [A] and [B] conducted in collaboration with Médecins sans Frontières and Epicenter</p> <p>Publication status: published</p> <p>Source: laboratory report obtained via SFM Microbiologie website</p>

Fourati 2020 [A] (Continued)

Author COI: 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Fourati 2020 [A] (Continued)

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

High risk

Fourati 2020 [B]
Study characteristics

Patient Sampling Comparative study of 6 Ag tests (no product codes reported); [Fourati 2020 \[A\]](#) reports full study characteristics and QUADAS

Patient characteristics and setting

Index tests Comparative study of 6 Ag tests (no product codes reported); [Fourati 2020 \[B\]](#) relates to test [B] in the list below; see [Fourati 2020 \[A\]](#) for full study characteristics and QUADAS entries

[A] SARS-CoV-2 COVID-19 Respi-Strip

[B] STANDARD Q COVID-19 Ag

[C] PanBio COVID-19 Antigen Rapid Test

[D] Biosynex COVID-19 Ag BSS

[E] COVID-VIRO Antigen Rapid Test

[F] NG Test SARS-CoV-2 Ag (assay excluded from review due to Vortex requirement as stated in IFU) (no product codes reported)

Manufacturer:

[A] Coris BioConcept, Gembloux, Belgium

[B] SD BIOSENSOR, Inc., Korea

[C] Abbott, Chicago, Illinois, USA

[D] Biosynex, Strasbourg, France

[E] AAZ, Boulogne-Billancourt, France

[F] NG Biotech, Guipry, France

Antibody: not stated

Ag target: not stated

Test method: not stated

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Fourati 2020 [B] *(Continued)*

Samples used: NP; collection not reported

Transport media: VTM (Cepheid or Deltalab); 100 µL used for testing

Sample storage: frozen at -80 °C until use

Test operator: laboratory staff

Definition of test positivity: visual, as per manufacturer IFU

Blinding reported: yes; each test was interpreted independently by 2 different laboratory technicians. A 3rd reading was carried out in the event of discrepancy

Timing of samples: pso (reported for 289 samples): 0-3 days 97, 34%; 4-7 days 103, 36%; 8-11 days 63, 22%; ≥ 12 days 26, 9%

Number of samples reported at > 7 days varied per test, maximum was 289

Target condition and reference standard(s)	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Comparative	
Notes	

Fourati 2020 [C]
Study characteristics

Patient Sampling	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Index tests	<p>Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [C] relates to test [C] in the list below; see Fourati 2020 [A] for full study characteristics and QUADAS entries</p> <p>[A] SARS-CoV-2 COVID-19 Respi-Strip [B] STANDARD Q COVID-19 Ag [C] PanBio COVID-19 Antigen Rapid Test [D] Biosynex COVID-19 Ag BSS [E] COVID-VIRO Antigen Rapid Test [F] NG Test SARS-CoV-2 Ag (assay excluded from review due to Vortex requirement as stated in IFU)</p> <p>Manufacturer:</p> <p>[A] Coris BioConcept, Gembloux, Belgium [B] SD BIOSENSOR, Inc., Korea [C] Abbott, Chicago, Illinois, USA [D] Biosynex, Strasbourg, France [E] AAZ, Boulogne-Billancourt, France [F] NG Biotech, Guipry, France</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Fourati 2020 [C] (Continued)

Test method: not stated

Samples used: NP; collection not reported

Transport media: VTM (Cepheid or Deltalab); 100 µL used for testing

Sample storage: frozen at -80 °C until use

Test operator: laboratory staff

Definition of test positivity: visual, as per manufacturer IFU

Blinding reported: yes; each test was interpreted independently by 2 different laboratory technicians. A 3rd reading was carried out in the event of discrepancy

Timing of samples: pso (reported for 289 samples): 0-3 days 97, 34%; 4-7 days 103, 36%; 8-11 days 63, 22%; ≥ 12 days 26, 9%

Number of samples reported at > 7 days varied per test, maximum was 289

Target condition and reference standard(s)	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Comparative	
Notes	

Fourati 2020 [D]

Study characteristics

Patient Sampling	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Index tests	<p>Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [D] relates to test [D] in the list below; see Fourati 2020 [A] for full study characteristics and QUADAS entries</p> <p>[A] SARS-CoV-2 COVID-19 Respi-Strip [B] STANDARD Q COVID-19 Ag [C] PanBio COVID-19 Antigen Rapid Test [D] Biosynex COVID-19 Ag BSS [E] COVID-VIRO Antigen Rapid Test [F] NG Test SARS-CoV-2 Ag (assay excluded from review due to Vortex requirement as stated in IFU)</p> <p>Manufacturer:</p> <p>[A] Coris BioConcept, Gembloux, Belgium [B] SD BIOSENSOR, Inc., Korea [C] Abbott, Chicago, Illinois, USA [D] Biosynex, Strasbourg, France [E] AAZ, Boulogne-Billancourt, France [F] NG Biotech, Guipry, France</p> <p>Antibody: not stated</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Fourati 2020 [D] (Continued)

Ag target: not stated

Test method: not stated

Samples used: NP; collection not reported

Transport media: VTM (Cepheid or Deltalab); 100 µL used for testing

Sample storage: frozen at -80 °C until use

Test operator: laboratory staff

Definition of test positivity: visual, as per manufacturer IFU

Blinding reported: yes; each test was interpreted independently by 2 different laboratory technicians. A 3rd reading was carried out in the event of discrepancy

Timing of samples: pso (reported for 289 samples): 0-3 days 97, 34%; 4-7 days 103, 36%; 8-11 days 63, 22%; ≥ 12 days 26, 9%

Number of samples reported at > 7 days varied per test, maximum was 289

Target condition and reference standard(s)	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
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Flow and timing	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
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Comparative

Notes

Fourati 2020 [E]
Study characteristics

Patient Sampling	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
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Patient characteristics and setting	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
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Index tests	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [E] relates to test [E] in the list below; see Fourati 2020 [A] for full study characteristics and QUADAS entries
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[A] SARS-CoV-2 COVID-19 Respi-Strip

[B] STANDARD Q COVID-19 Ag

[C] PanBio COVID-19 Antigen Rapid Test

[D] Biosynex COVID-19 Ag BSS

[E] COVID-VIRO Antigen Rapid Test

[F] NG Test SARS-CoV-2 Ag (assay excluded from review due to Vortex requirement as stated in IFU)

Manufacturer:

[A] Coris BioConcept, Gembloux, Belgium

[B] SD BIOSENSOR, Inc., Korea

[C] Abbott, Chicago, Illinois, USA

[D] Biosynex, Strasbourg, France

[E] AAZ, Boulogne-Billancourt, France

[F] NG Biotech, Guipry, France

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Fourati 2020 [E] (Continued)

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: NP; collection not reported

Transport media: VTM (Cepheid or Deltalab); 100 µL used for testing

Sample storage: frozen at -80 °C until use

Test operator: laboratory staff

Definition of test positivity: visual, as per manufacturer IFU

Blinding reported: yes; each test was interpreted independently by 2 different laboratory technicians. A 3rd reading was carried out in the event of discrepancy

Timing of samples: pso (reported for 289 samples): 0-3 days 97, 34%; 4-7 days 103, 36%; 8-11 days 63, 22%; ≥ 12 days 26, 9%

Number of samples reported at > 7 days varied per test, maximum was 289

Target condition and reference standard(s)	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 6 Ag tests (no product codes reported); Fourati 2020 [A] reports full study characteristics and QUADAS
Comparative	
Notes	

Garcia-Finana 2021

Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: asymptomatic individuals attending asymptomatic testing sites (ATS) in Liverpool were asked to participate in a QA process</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 5869 (74)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centres (asymptomatic)</p> <p>Location: 48 testing sites in Liverpool</p> <p>Country: UK</p> <p>Dates: 8-29 November 2020</p> <p>Symptoms and severity: asymptomatic</p> <p>Demographics: mean age 50 years (SD 18 years), 54% women, 82% white ethnicity</p>

Garcia-Finana 2021 (Continued)

	Exposure history: not reported
Index tests	<p>Test name: Innova SARS-CoV-2 antigen LFD</p> <p>Manufacturer: Innova Medical Group</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: not stated; self-collected (presume nasal + OP), LFT swab obtained first</p> <p>Transport media: none used</p> <p>Sample storage: no storage</p> <p>Test operator: trained non-HCW (assumed)</p> <p>Definition of test positivity: visual line appearance</p> <p>Blinding reported: yes; conducted first</p> <p>Timing of samples: asymptomatic</p>
Target condition and reference standard(s)	<p>Reference standard: PCR; "standard test used in Lighthouse Laboratories"</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): N, S, ORF1 (from Table 2)</p> <p>Samples used: nasal + OP; swab for PCR obtained second</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous; paired</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes</p> <p>Uninterpretable results: void results: LFT: 22 (4 PCR+ and 18 PCR-) PCR: 343 (2 LFT+ and 341 LFT-)</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "the evaluation was invited by the joint local and national command of the pilot and sponsored by the Department of Health and Social Care (DHSC)"</p> <p>Publication status: published</p>

Garcia-Finana 2021 (Continued)

Source: published report (interim)

Author COI: none 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			

Garcia-Finana 2021 (Continued)

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

Gomez 2021(a)
Study characteristics

Patient Sampling	<p>Report of 2 study cohorts. This entry Gomez 2021(a) relates to cohort [1]: [1] single-group study estimating sensitivity and specificity in symptomatic paediatric patients presenting at outpatients or in primary care (all < 18 years); total n = 427 Second cohort [2], included as included as Gomez 2021(b):</p> <p>[2] single-group study estimating sensitivity alone in a symptomatic PCR+ student/college-aged population (18-25 years) presenting at a university campus; total n = 32 (A further 3 groups were reported but did not undergo Ag testing and were excluded from the review: [3] ED-collected specimens; [4] asymptomatic people undergoing surgical procedures unrelated to COVID-19; [5] asymptomatic students)</p> <p>Recruitment: not reported</p> <p>Prospective or retrospective: not reported</p> <p>Sample size (cases): 427 (43)</p>
Patient characteristics and setting	<p>Setting: community outpatients or primary care</p> <p>Location: UPMC Children's Community Pediatrics and UPMC Children's Hospital of Pittsburgh Primary Care Center</p> <p>Country: USA (Pennsylvania)</p> <p>Dates: 8 March-10 September 2020</p> <p>Symptoms and severity: symptoms not reported Reported as "symptomatic" and "presented for care"</p> <p>Demographics: age and sex not reported</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Sofia 2 SARS Antigen used in Group [1]</p> <p>Manufacturer: Quidel (USA)</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: FIA</p> <p>Samples used: direct swabs NMT (collection not reported)</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gomez 2021(a) (Continued)

	<p>Transport media: none used</p> <p>Sample storage: not reported; probably immediate, testing conducted on site</p> <p>Test operator: not reported ("performed according to CLIA'88 regulations by appropriate personnel")</p> <p>Definition of test positivity: not reported; as per manufacturer IFU</p> <p>Blinding reported: most likely. Index test was done on site and reference test samples were transported to lab.</p> <p>Timing of samples: not reported</p>
Target condition and reference standard(s)	<p>Reference standard: laboratory-developed test based on the CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel EUA (CDC) protocol Run per the manufactures' IFU</p> <p>Definition of non-COVID cases: as for cases</p> <p>Genetic target(s): not reported</p> <p>Samples used: same as for index test; NMT</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous, paired swabs</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "this study was enabled by internal funding provided by UPMC Hospital System and the University of Pittsburgh"</p> <p>Publication status: preprint (not peer reviewed)</p> <p>Source: preprint server (medRxiv)</p> <p>Author COI: no COI statement reported</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Gomez 2021(a) *(Continued)*

Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gomez 2021(a) *(Continued)*

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Gomez 2021(b)
Study characteristics

Patient Sampling	<p>Report of 2 study cohorts. This entry Gomez 2021(b) relates to cohort [2]: [2] single-group study reporting only sensitivity in symptomatic PCR+ student/college-aged population (18-25 years) presenting at a university campus; total n = 32</p> <p>Second cohort [1] included as included as Gomez 2021(a): [1] single-group study estimating sensitivity and specificity in symptomatic paediatric patients presenting at out-patients or in primary care (all < 18 years); total n = 427 (A further 3 groups were reported but did not undergo Ag testing and were excluded from the review: [3] ED-collected specimens; [4] asymptomatic persons undergoing surgical procedures unrelated to COVID-19; [5] asymptomatic students)</p> <p>Recruitment: randomly selected</p> <p>Prospective or retrospective: not reported</p> <p>Sample size (cases): 32 (32); number of PCR-ve students was not reported (consider author contact)</p>
Patient characteristics and setting	<p>Setting: student health services</p> <p>Location: Pittsburgh campus of the University of Pittsburgh</p> <p>Country: USA (Pennsylvania)</p> <p>Dates: 8 March-10 September 2020</p> <p>Symptoms and severity: symptoms not reported Reported as "symptomatic" and "presented for care"</p> <p>Demographics: age and sex not reported</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: BD Veritor SARS-CoV-2 used in group [2]</p> <p>Manufacturer: BD (USA)</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: unknown; LFA not otherwise described</p> <p>Samples used: direct swabs AN (collection not reported)</p> <p>Transport media: none used</p> <p>Sample storage: not reported; probably immediate</p>

Gomez 2021(b) (Continued)

	<p>Test operator: not reported ("performed according to CLIA'88 regulations by appropriate personnel")</p> <p>Definition of test positivity: not reported; as per manufacturer IFU</p> <p>Blinding reported: most likely. Index test was done on site and reference test samples were transported to lab.</p> <p>Timing of samples: not reported</p>
Target condition and reference standard(s)	<p>Reference standard: GeneXpert Xpress SARS-CoV-2 assay (Cepheid Inc) or Laboratory-Developed Test based on the CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel EUA (CDC) protocol</p> <p>Run per the manufacturer's IFU</p> <p>Definition of non-COVID cases: N/A</p> <p>Genetic target(s): not reported</p> <p>Samples used: same as for index test; AN</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous, paired swabs</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "this study was enabled by internal funding provided by UPMC Hospital System and the University of Pittsburgh"</p> <p>Publication status: preprint (not peer reviewed)</p> <p>Source: preprint server (medRxiv)</p> <p>Author COI: no COI statement reported</p>

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?	No		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gomez 2021(b) (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gomez 2021(b) *(Continued)*

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Gonzalez-Donapetry 2021
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity in symptomatic children meeting COVID-19 clinical criteria and presenting < 7 days pso

Recruitment: unclear

Prospective or retrospective: prospective

Sample size (cases): 440 (18)

Patient characteristics and setting Setting: paediatric ED

Location: Madrid (Hospital Universitario La Paz)

Country: Spain

Dates: 25 September-14 October 2020

Symptoms and severity: all symptomatic: n = 440
 Symptoms included: cough 222 (51%), fever 296 (67%), dyspnoea 67 (15%), headache 35 (8%), dysgeusia/anosmia 1 (0%), odynophagia 55 (13%), rhinorrhoea 228 (52%), gastrointestinal disorder 103 (23%)

Demographics: med age (IQR): 3 (1-7)
 Male: 260 (59%)
 female: 180 (41%)

Exposure history: not reported

Index tests Test name: Panbio COVID-19 Ag Rapid Test

Manufacturer: Abbott Rapid Diagnostics Jena GmbH

Antibody: SARS-CoV-2 nucleoprotein antigens

Ag target: immobilized anti-SARS-CoV-2 antibody

Test method: membrane technology with gold conjugate CGIA

Samples used: NP (no further detail reported)

Transport media: none

Sample storage: assume immediate testing (no transport or storage reported)

Test operator: not reported

Definition of test positivity: according to manufacturer's protocol

Blinding reported: yes (based on timing of tests)

Gonzalez-Donapetry 2021 (Continued)

	Timing of samples: med time since symptoms onset (IQR): total: 1 (1-3) days; PCR- 1 (1-3); PCR+ 1 (1-2)
Target condition and reference standard(s)	<p>Reference standard: Vircell SARS-CoV-2 real-time PCR kit (Vircell, Granada, Spain); ≤ 40 Ct considered positive</p> <p>Definition of non-COVID cases: as for cases</p> <p>Genetic target(s): nucleocapsid (N) and envelope (E) genes</p> <p>Samples used: NP swab samples collected in Universal Transport Medium, COPAN Italia or DeltaSwab Virus, Deltalab (different swab from index test)</p> <p>Timing of reference standard: same as for index test</p> <p>Blinded to index test: not reported</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: appears simultaneous</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: no funding to disclose</p> <p>Publication status: published paper</p> <p>Source: Pediatric Infectious Disease Journal</p> <p>Author COI: authors declare no COI present</p>

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 inclusions?	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

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gonzalez-Donapetry 2021 (Continued)

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Gremmels 2021(a)
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gremmels 2021(a) (Continued)

Patient Sampling	<p>Report of 2 cohorts of patients presenting for COVID-19 testing. Gremmels 2021(a) entry relates to: [1] community-dwelling mildly symptomatic subjects in a medium endemic area (n = 1369)</p> <p>Gremmels 2021(b) entry reports data for second cohort [2], in a high endemic area</p> <p>Recruitment: yes; all individuals invited to participate</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: community testing centre</p> <p>Location: [1] University Medical Center Utrecht (UMCU)</p> <p>Country: Netherlands</p> <p>Dates: [1] 22 September-6 October</p> <p>Symptoms and severity: cohort [1] only. Data on symptoms were missing from 9 participants Asymptomatic 37, 2.7%, sore throat 907, 66.3%; coryza 943, 69%; cough 780, 57.1%; headache 601, 44.0%; tiredness 565, 41.3%; general malaise 365, 26.7% (further 19 documented)</p> <p>Demographics: median age 36.4 years (IQR 27.0-49.6 years); 523, 38.3% male</p> <p>Exposure history: 233, 17% contact with confirmed case</p>
Index tests	<p>Test name: Panbio COVID-19 Ag Rapid Test (lot 41ADF011A)</p> <p>Manufacturer: Abbott (Lake Country, IL, U.S.A)</p> <p>Antibody: NP</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP; obtained after NOP swab for RT-PCR; implies collected by HCW</p> <p>Transport media: unclear; states transferred to 3 mL UTM after collection until further processing but also describes collected swabs transferred into dedicated sample collection tubes containing a sampling buffer for Ag test</p> <p>Sample storage: none; swabs transported to the laboratory (5 min walking distance from the sampling location) and tested within 2 h of collection</p> <p>Test operator: 2 independent observers, samples processed in a level 2 biosafety cabinet</p> <p>Definition of test positivity: visual line within 15 min; as per manufacturer IFU</p> <p>Blinding reported: yes; observers (blinded to each other and to the PCR results)</p> <p>Timing of samples: cohort [1] (data on duration of symptoms reportedly missing for 201 participants; total reported here is 1138 but denominator for %s is 1166) Day 1-3 387, 33.2%; day 4-7 560, 48.0%; day > 7 191, 16.4%</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Seegene Allplex</p> <p>Positive result on amplification of any of the 3 SARS-CoV-2 genes</p> <p>Definition of non-COVID cases: as for cases; single negative result</p> <p>Genetic target(s): E-, N-, and RdRP-gene</p> <p>Samples used: NOP (paired)</p>

Gremmels 2021(a) (Continued)

Timing of reference standard: NOP swab obtained first for RT-PCR

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired

All participants received same reference standard: yes

Missing data: 2 patients excluded ("inappropriate application of NP swab and lab mislabelling"), disease status not reported. (Considered overall low risk of bias due to small numbers)

Uninterpretable results: none reported

Indeterminate results (index test): none; no bands were classified as unclear by the independent observers

Indeterminate results (reference standard): patients

Unit of analysis: participant

Comparative

Notes

Funding: No external funding

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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		

Gremmels 2021(a) *(Continued)*

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Gremmels 2021(b)
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gremmels 2021(b) (Continued)

Patient Sampling	<p>Report of 2 cohorts of patients presenting for COVID-19 testing. Gremmels 2021(b) entry relates to: [2] community-dwelling mildly symptomatic people in a high endemic area (n = 208)</p> <p>Gremmels 2021(a) entry reports data for second [1], cohort in a medium endemic area</p> <p>Recruitment: yes; all individuals invited to participate</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: community testing centre</p> <p>Location: [2] Horacio Oduber Hospital on Aruba</p> <p>Country: Netherlands</p> <p>Dates: [2] 23 September-9 October</p> <p>Symptoms and severity: not stated; "mildly symptomatic", presume mixed as per 2020 preprint by Gremmels (see secondary reference under Gremmels 2021(b)).</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Panbio COVID-19 Ag Rapid Test (lot 41ADF011A)</p> <p>Manufacturer: Abbott (Lake Country, IL, USA)</p> <p>Antibody: NP</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP; obtained after NOP swab for RT-PCR; implies collected by HCW</p> <p>Transport media: no UTM used for Ag samples; collected swabs transferred into dedicated sample collection tubes containing a sampling buffer</p> <p>Sample storage: none; swabs transported to the laboratory (5 min walking distance from the sampling location) and tested within 2 h of collection</p> <p>Test operator: 2 independent observers, samples processed in a level 2 biosafety cabinet</p> <p>Definition of test positivity: visual line within 15 min; as per manufacturer IFU</p> <p>Blinding reported: yes; observers (blinded to each other and to the PCR results)</p> <p>Timing of samples: not stated; on presentation</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Seegene Allplex</p> <p>Positive result = amplification of any of the 3 SARS-CoV-2 genes</p> <p>Definition of non-COVID cases: as for cases; single negative result</p> <p>Genetic target(s): E-, N-, and RdRP-gene</p> <p>Samples used: NOP (paired)</p> <p>Timing of reference standard: NOP swab obtained first for RT-PCR</p> <p>Blinded to index test: not stated</p>

Gremmels 2021(b) *(Continued)*

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired

All participants received same reference standard: yes

Missing data: none reported for Aruba site

Uninterpretable results: none reported

Indeterminate results (index test): none; no bands were classified as unclear by the independent observers

Indeterminate results (reference standard): none

Unit of analysis: participant

Comparative

Notes

Funding: No external funding

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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Gremmels 2021(b) *(Continued)*

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Gupta 2020
Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity: symptomatic patients with suspected COVID-19 and asymptomatic contacts of laboratory-confirmed cases between 5 and 10 days of exposure, meeting Indian Council of Medical Research (ICMR) strategy for COVID-19 testing Recruitment: consecutive Prospective or retrospective: not stated; appears prospective
Patient characteristics and setting	Setting: outpatient (tertiary care hospital)

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gupta 2020 (Continued)

Location: All India Institute of Medical Sciences (AIIMS), New Delhi

Country: India

Dates: 31 May-24 July 2020

Symptoms and severity: 204 (62%) symptomatic; 126 (38%) asymptomatic
Median symptom duration: 1 day (range: 1-10). Symptoms included: fever (31.5%), cough (25.4%), fatigue/malaise (11.8%), headache (3.3%), runny nose (3.3%)

Demographics: median age 34.1 ± 12.6 years; 231 (70%) male

Exposure history: 127 asymptomatic were in contact with confirmed case

Index tests

Test name: STANDARD Q rapid antigen detection test

Manufacturer: SD Biosensor, Inc., Gurugram

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: NP; collection method detailed but personnel not described; presume HCW. Sequence for specimen collection was random for both the samples (Ag and RT-PCR)

Transport media: none

Sample storage: none

Test operator: same person who obtained swab; HCW

Definition of test positivity: visual; test and control lines

Blinding reported: yes; conducted first

Timing of samples: symptomatic: 192 (95%) ≤ 5 days pso (including 57 cases)

Target condition and reference standard(s)

Reference standard: RT-PCR; commercial assay (BGI Genomics Co. Ltd., China). Psoitive defined as per manufacturer IFU

Definition of non-COVID cases: as for cases; single negative

Genetic target(s): ORF1 ab

Samples used: nasal and throat swabs (NOP) in VTM

Timing of reference standard: as for index test; states the sequence for specimen collection was random for both the samples

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous; paired swabs

All participants received same reference standard: yes

Missing data: none reported, no participant flow diagram reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Gupta 2020 (Continued)

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: "financially supported by the Indian Council of Medical Research, New Delhi (for the Regional Virus Research and Diagnostic Laboratory at the All India Institute of Medical Sciences, New Delhi)"

Publication status: published

Source: Indian Journal of Medical Research

Author COI: author report no COI present

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Yes		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate inclusions?	Yes		
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Could the selection of patients have introduced bias?		Low risk	
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Are there concerns that the included patients and setting do not match the review question?			Low concern
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DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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If a threshold was used, was it pre-specified?	Yes		
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Could the conduct or interpretation of the index test have introduced bias?		Low risk	
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Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
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DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	No		
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gupta 2020 (Continued)

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Halfon 2021
Study characteristics

Patient Sampling	2-group study estimating sensitivity and specificity: [1] RT-PCR positive (n = 100) [2] RT-PCR negative (n = 100) Selected from 43,399 samples that had undergone RT-qPCR for SARS-CoV-2 using NP swab Recruitment: unclear; selected "considering the distribution of both TSO (time after symptom onset) and Cts" Prospective or retrospective: prospectively Sample size (cases): 200 (100)
Patient characteristics and setting	Setting: laboratory-based Location: Marseille; author institutions Hôpital Européen Marseille Country: France Dates: August-November 2020

Halfon 2021 (Continued)

	<p>Symptoms and severity: (Figure 1) 104 (52%) asymptomatic, including 35 PCR+; 69 (35%) symptomatic, including 18 PCR+; 27 (13%) symptom status unknown or time not reported, including 13 PCR+</p> <p>Demographics: mean age 48 years (SD 21); 96 male (48%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Panbio COVID 19 antigen rapid test</p> <p>Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany</p> <p>Antibody: SARS-CoV-2 nucleocapsid protein</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: NP swabs; collection not described</p> <p>Transport media: not stated</p> <p>Sample storage: not stated</p> <p>Test operator: not stated</p> <p>Definition of test positivity: not stated</p> <p>Blinding reported: not stated</p> <p>Timing of samples: for symptomatic, time pso was: ≤ 4 days 47, > 4 days 22, and not reported or unknown 27</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; UltraGene Combo2Screen SARS-CoV-2 Assay and Chemagic™ viral DNA/RNA 300 kit H96 (ref. CMG-1033-S) on a Chemagic™ 360-D instrument (PerkinElmer, Inc., Austin, TX)</p> <p>Ct values for positive cases plotted up to 37 Ct (Figure 2)</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP swabs</p> <p>Timing of reference standard: not stated; same as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: not stated; presume simultaneous as same swab seems to have been used</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>

Halfon 2021 (Continued)

Comparative

Notes	Funding: no funding source
	Publication status: preprint
	Source: medRxiv
	Author COI: No COI statement provided

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Halfon 2021 *(Continued)*

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Unclear risk

Houston 2021
Study characteristics

Patient Sampling

Single-group study estimating sensitivity and specificity: adult admissions who met the WHO COVID-19 case definition at a busy acute hospital

Recruitment: not stated; appears to be all meeting eligibility criteria

Prospective or retrospective: prospective

Sample size (cases): 728 (280)

Patient characteristics and setting

Setting: inpatient

Location: Northwick Park Hospital

Country: UK

Dates: 17 November-31 December 2020

Symptoms and severity: all symptomatic (as per WHO case definition); required supplemental oxygen, n (%; 95% CI) 141 (21.4%, 18.3-24.6); temperature > 38 °C, n (%; 95% CI) 163 (24.9%, 21.6-28.2)

Demographics: median age 67.5 years (IQR 52-82); 327 (44.9%) female

Exposure history: not stated

Index tests

Test name: Innova SARS-CoV-2 Antigen Rapid Qualitative Test

Manufacturer: Lotus Global Company, London, UK

Antibody: not stated

Ag target: not stated

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Houston 2021 (Continued)

	Test method: CGIA Samples used: NP swabs; collection not described Transport media: not stated; immediate testing Sample storage: none; immediate testing Test operator: appropriately trained healthcare assistants in the ED Definition of test positivity: not stated Blinding reported: yes, conducted first Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR; no details Definition of non-COVID cases: as for cases; single negative Genetic target(s): not stated Samples used: NP swabs (paired) Timing of reference standard: same as for index test Blinded to index test: not stated Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swab All participants received same reference standard: yes Missing data: not stated; only valid results included Uninterpretable results: none Indeterminate results (index test): none Indeterminate results (reference standard): none Unit of analysis: participant
Comparative	
Notes	Funding: no specific grant Publication status: published Source: Journal of Hospital Infection Author COI: no competing interests 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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Houston 2021 (Continued)

Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Huh 2021

Study characteristics

Patient Sampling	<p>Unclear design estimating sensitivity and specificity: included samples PCR positive or negative for SARS-CoV-2 (A second study evaluating serology assays for antibody detection in additional PCR+ and pre-pandemic samples was also reported but not eligible for this review)</p> <p>Recruitment: unclear</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 132 (62)</p>
Patient characteristics and setting	<p>Setting: stated "2 institutions", no further details reported</p> <p>Location: not reported; authors' institutions include Dongguk University Ilsan hospital and College of Medicine, Chosun University</p> <p>Country: not stated; appears to be Korea</p> <p>Dates: not reported</p> <p>Symptoms and severity: not reported; could all be symptomatic as data are reported up to 12 days pso for PCR+ only</p> <p>Demographics: age and sex not reported</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: PCL COVID19 Ag Rapid FIA used with the PCLOK EZ analyzer</p> <p>Manufacturer: PCL Inc.</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: FIA</p> <p>Samples used: NP (collection not reported)</p> <p>Transport media: VTM (further details not reported)</p> <p>Sample storage: storage in VTM reported, test done after reference standard, but exact timing not reported</p> <p>Test operator: not reported</p> <p>Definition of test positivity: not reported</p> <p>Blinding reported: appears to be no (index test after reference standard)</p> <p>Timing of samples: 0-12 days pso (n = 62) Results reported for 0-7 days (n = 48) and 8-12 days (n = 14) periods</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; PowerChek™2019-nCoV Real-time PCR Kit, Kogenebiotech, Seoul, 22 Korea</p> <p>Study also reports use of the RT-PCR CFX96 Real-time PCR detection system (Bio-Rad Laboratories, Hercules, CA) with the Allplex 2019-nCoV Assay kit (Seegene Inc., Seoul, Korea), however this appears to relate to the evaluation of serological tests</p> <p>Definition of non-COVID cases: as for cases</p>

Huh 2021 (Continued)

Genetic target(s): RdRP and N genes specific for 2 SARS-CoV-2 and E gene for all of sarbecovirus including SARS-CoV-2

Samples used: NP swabs, appears to be same as for index test

Timing of reference standard: appears to be same as index test

Blinded to index test: yes (index test after reference)

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: appears to be simultaneous, as samples were stored and reference test was done before index test; however 2 PCR assays are reported and it is not clear whether a second PCR may be have been carried out?

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative
Notes

Funding: "supported by the Promising IP Project Support Program funded by the Ministry of Trade Industry and Energy. And this study was supported by the Clinical Trial Support Program funded by the Ministry of Health and Warfare. Also, this study was supported by the Technological Innovation R&D Program funded by the Korea Health Industry Development Institute (KHIDI)."

Publication status: preprint (not peer reviewed)

Source: preprint server (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?	Unclear		
Did the study avoid inappropriate inclusions?	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

Huh 2021 (Continued)

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Huh 2021 (Continued)

Could the patient flow have introduced bias?

Unclear risk

Igloi 2021

Study characteristics

Patient Sampling	<p>Multi-group study to estimate sensitivity and specificity including: [1] symptomatic RT-PCR test-positive patients (n = 160) [2] exposed HCWs and patient contacts (n = 150) Data are presented only for groups [1] and [2] combined; author contacted 15 March 2021</p> <p>Recruitment: unclear (do not state all patients)</p> <p>Prospective or retrospective: not stated; appears prospective</p> <p>Sample size (cases): 310 (188)</p>
Patient characteristics and setting	<p>Setting: mixed; described as patients, their contacts and exposed HCWs</p> <p>Location: Fayoum University Hospital, Fayoum</p> <p>Country: Egypt</p> <p>Dates: May 2020</p> <p>Symptoms and severity: unclear; 160 PCR+ve "patients" presumably symptomatic, plus 150 presumably asymptomatic contacts and exposed HCWs</p> <p>Demographics: median age 42 years; 184/310 (59%) male</p> <p>Exposure history: states "exposed healthcare workers and patient contacts."; no further details</p>
Index tests	<p>Test name: BIOCREDIT COVID-19 Ag kit</p> <p>Manufacturer: not stated; manufacturer is RapiGEN</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA; described as lateral flow immunochromatographic assay (uses a dual-colour system for the qualitative detection of the SARS-CoV-2 antigen)</p> <p>Samples used: NP using flocked swabs; collection not otherwise specified</p> <p>Transport media: UTM (UTM-RT System, Copan Diagnostics, Murrieta, CA)</p> <p>Sample storage: transported to lab within 1-2 h of collection; then stored at 4 °C and tested within 24 h</p> <p>Test operator: laboratory staff</p> <p>Definition of test positivity: no details</p> <p>Blinding reported: unclear; index test performed after PCR test</p> <p>Timing of samples: group [1] (n = 160); median 3 days pso</p>

Igloi 2021 (Continued)

Target condition and reference standard(s)	Reference standard: RT-PCR (multiplex real-time PCR detection kit; DTlite 4, Russia) Definition of non-COVID cases: as for cases; single negative Genetic target(s): not stated Samples used: NP in VTM; same as for index test Timing of reference standard: as for index test Blinded to index test: yes (PCR performed before index test) Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; same swab All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: no external funding Publication status: published Source: Laboratory Medicine Author COI: author report 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 inclusions?	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 (Evaluations of single test application)			

Igloi 2021 (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Ishii 2021 [A]
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Ishii 2021 [A] (Continued)

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: samples submitted for COVID-19 diagnosis at a medical centre; includes symptomatic patients (dysosmia, dysgeusia, fever and pneumonia) and asymptomatic close contacts of confirmed cases</p> <p>Recruitment: unclear; all samples had PCR and Lunmpulse, whereas the Espline test was performed on randomly selected samples</p> <p>Prospective or retrospective: unclear; NP swabs and saliva samples were collected from 33 COVID-19 patients and 564 non-COVID-19 patients</p> <p>Sample size (cases): [A]: NP swabs: 271 (11); [B]: saliva samples: 93 (9)</p>
Patient characteristics and setting	<p>Setting: unclear</p> <p>Location: Toho University Omori Medical Center</p> <p>Country: Japan</p> <p>Dates: August-September 2020</p> <p>Symptoms and severity: all PCR+ cases with an ESPLINE result were symptomatic (n = 20)</p> <p>Demographics: not stated</p> <p>Exposure history: no details reported</p>
Index tests	<p>Test name: Espline SARS-CoV-2</p> <p>Manufacturer: Fujirebio Inc., Tokyo, Japan</p> <p>Antibody: viral nucleocapsid antigen</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: [A]: NP and [B]: saliva samples (not reported who collected by)</p> <p>Transport media: not reported (Saliva samples were diluted 2-fold with dedicated reagent. The sample solution was centrifuged at 12,000 rpm for 2 min)</p> <p>Sample storage: unfrozen and fresh</p> <p>Test operator: not reported</p> <p>Definition of test positivity: positive line observed with naked eye</p> <p>Blinding reported: unclear</p> <p>Timing of samples: [A]: 10/11 within 2 days pso, 1/11 at 4 days pso [B]: 7/9 within 7 days pso and 2/9 within 8-14 days pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; TaqMan Fast Virus 1-step Master Mix (Thermo Fisher Scientific, Waltham, MA, USA) on the QuantStudio 5 Real-Time PCR System (Thermo Fisher Scientific)</p> <p>Ct < 35 considered positive</p> <p>Definition of non-COVID cases: as for cases</p> <p>Genetic target(s): not reported</p> <p>Samples used: same as for index test</p>

Ishii 2021 [A] (Continued)

Timing of reference standard: same as for index test

Blinded to index test: unclear

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous (same swab)

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: no specific grant funding

Publication status: published paper

Source: Journal of Infection and Chemotherapy

Author COI: declaration of competing interest: none

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Unclear		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate inclusions?	Unclear		
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Could the selection of patients have introduced bias?		Unclear risk	
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Are there concerns that the included patients and setting do not match the review question?			Unclear
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DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
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If a threshold was used, was it pre-specified?	Yes		
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Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Ishii 2021 [A] (Continued)

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Ishii 2021 [B]
Study characteristics

Patient Sampling Comparative study of an Ag using 2 different samples; [Ishii 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of an Ag using 2 different samples; [Ishii 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Test name: Espline SARS-CoV-2
Manufacturer: Fujirebio Inc., Tokyo, Japan

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Ishii 2021 [B] (Continued)

Antibody: viral nucleocapsid antigen

Ag target: not reported

Test method: not reported

 Samples used: [A]: NP and **[B]: saliva samples** (not reported who collected by)

Transport media: not reported

(Saliva samples were diluted 2-fold with dedicated reagent. The sample solution was centrifuged at 12,000 rpm for 2 min)

Sample storage: unfrozen and fresh

Test operator: not reported

Definition of test positivity: positive line observed with naked eye

Blinding reported: unclear

Timing of samples: [A]: 10/11 within 2 days pso, 1/11 at 4 days pso

[B]: 7/9 within 7 days pso and 2/9 within 8-14 days pso

Target condition and reference standard(s)	Comparative study of an Ag using 2 different samples; Ishii 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of an Ag using 2 different samples; Ishii 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of an Ag using 2 different samples; Ishii 2021 [A] reports full study characteristics and QUADAS.

Jaaskelainen 2021 [A]
Study characteristics

Patient Sampling	<p>Multi-group study to estimate sensitivity and specificity including:</p> <p>[1] RT-PCR test-positive samples from adults from outpatient clinics and drive-through testing sites (n = 96) {Additional cohort [2] RT-PCR+ve and negative samples for analysis of analytical performance (n = 102); excluded as they were deliberately selected to cover a wide Ct range (26.35-32.66 Ct)}</p> <p>Recruitment: [1] appears consecutive (selected "systematically backward")</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 136 (96); different number of cases tested per assay</p>
Patient characteristics and setting	<p>Setting: outpatient/community test centre drive-through testing sites</p> <p>Location: HUS Diagnostic Center, Helsinki University Hospital, Helsinki</p> <p>Country: Finland</p> <p>Dates: [1] 1-18 November 2020</p>

Jaaskelainen 2021 [A] (Continued)

Symptoms and severity: not stated

Demographics: not stated

Exposure history: not stated

Index tests

Test name:

[A] Quidel Sofia SARS FIA (lots used 143489)

[B] STANDARD Q COVID-19 Ag test (lots used QCO3020105)

[C] Panbio (lots used 41ADF024A)

All 3 were CE IVD marked SARS-CoV-2 RADTs

Manufacturer:

[A] Quidel, San Diego, CA

[B] SD Biosensor, Republic of Korea

[C] Abbott Diagnostic GmbH, Jena, Germany

Antibody: Ag (nucleocapsid protein)

Ag target: NA

 Test method: **[A] FIA** ; [B] and [C] not stated

Samples used: NP swabs (not reported who collected the sample)

Transport media: stored in 0.9% saline; authors note this is "off-label" use of the assays

Sample storage: stored at -20 °C

Test operator: not stated; presume laboratory staff

 Definition of test positivity: **[A] detection of fluorescent signal**; [B] and [C] appearance of visible line

Blinding reported: unclear/details not reported. Probably no (positive/negative samples were selected based on the RT-PCR tests for performance tests)

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: RT-PCR; in-house (laboratory-developed test using modified method by Corman et al)

Virus culture also used for PCR positive subset of samples

Definition of non-COVID cases: NA

Genetic target(s): N gene target of SARS-CoV-2

Samples used: NP swabs; same as for index test

Timing of reference standard: not reported

Blinded to index test: yes; PCR conducted for diagnosis prior to sample storage

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous (same swab)

All participants received same reference standard: yes

Missing data: number of samples tested varied by assay. Of 96 PCR+ samples in group [1], results were reported for:

1. Sofia (Quidel): 87 samples, 91%

Jaaskelainen 2021 [A] (Continued)

2. STANDARD Q (SD Biosensor): 96 samples, 100%
3. Panbio (Abbott): 90 samples, 94%

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: not stated; no indication of multiple samples per patient

Comparative

Notes

Funding: not reported

Publication status: preprints

Source: medRxiv

Author COI: not reported

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	No		
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Was a case-control design avoided?	No		
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Did the study avoid inappropriate inclusions?	Yes		
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Could the selection of patients have introduced bias?		High risk	
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Are there concerns that the included patients and setting do not match the review question?			High
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DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
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If a threshold was used, was it pre-specified?	Yes		
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Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
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Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
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DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Jaaskelainen 2021 [A] (Continued)

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Jaaskelainen 2021 [B]
Study characteristics

Patient Sampling	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Index tests	Test name: [A] Quidel Sofia SARS FIA (lots used 143489) [B] STANDARD Q COVID-19 Ag test (lots used QCO3020105) [C] Panbio (lots used 41ADF024A) All 3 were CE IVD marked SARS-CoV-2 RADTs Manufacturer:

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Jaaskelainen 2021 [B] *(Continued)*

[A] Quidel, San Diego, CA

[B] SD Biosensor, Republic of Korea

[C] Abbott Diagnostic GmbH, Jena, Germany

Antibody: Ag (nucleocapsid protein)

Ag target: NA

Test method: [A] FIA; **[B] and [C] not stated**

Samples used: NP swabs (not reported who collected the sample)

Transport media: stored in 0.9% saline; authors note this is "off-label" use of the assays

Sample storage: stored at -20 °C

Test operator: not stated; presume laboratory staff

Definition of test positivity: [A] detection of fluorescent signal; [B] and [C] appearance of visible line

Blinding reported: unclear/details not reported. Probably no (positive/negative samples were selected based on the RT-PCR tests for performance tests)

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.

Jaaskelainen 2021 [C]
Study characteristics

Patient Sampling	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] Quidel Sofia SARS FIA (lots used 143489) [B] STANDARD Q COVID-19 Ag test (lots used QCO3020105) [C] Panbio (lots used 41ADF024A) All 3 were CE IVD marked SARS-CoV-2 RADTs</p> <p>Manufacturer:</p> <p>[A] Quidel, San Diego, CA [B] SD Biosensor, Republic of Korea [C] Abbott Diagnostic GmbH, Jena, Germany</p> <p>Antibody: Ag (nucleocapsid protein)</p> <p>Ag target: NA</p>

Jaaskelainen 2021 [C] *(Continued)*

 Test method: [A] FIA; **[B] and [C] not stated**

Samples used: NP swabs (not reported who collected the sample)

Transport media: stored in 0.9% saline; authors note this is "off-label" use of the assays

Sample storage: stored at -20 °C

Test operator: not stated; presume laboratory staff

Definition of test positivity: [A] detection of fluorescent signal; [B] and [C] appearance of visible line

Blinding reported: unclear/details not reported. Probably no (positive/negative samples were selected based on the RT-PCR tests for performance tests)

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 Ag tests; Jaaskelainen 2021 [A] reports full study characteristics and QUADAS.

Jakobsen 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: symptomatic and asymptomatic patients (self-reported) who had booked an appointment at a public test centre</p> <p>Recruitment: consecutive (all who appeared for the appointment were tested)</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 4697 patients with 4811 paired conclusive tests (221 tests); 196 were tested twice or more</p>
Patient characteristics and setting	<p>Setting: public COVID-19 test centre</p> <p>Location: not stated; author institution is University of Copenhagen, Copenhagen</p> <p>Country: Denmark</p> <p>Dates: 26-31 December 2020</p> <p>Symptoms and severity: 705 (15%) symptomatic (self-report); 3008 (64%) asymptomatic (Not all participants responded to the online questionnaire regarding symptoms)</p> <p>Demographics: mean age 45 (SD 16.9) years; 2456 (53%) female</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag test</p> <p>Manufacturer: SD BIOSENSOR</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Jakobsen 2021 (Continued)

	<p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: NP (states test "performed" by personnel from private company at the test centre, no detail of swab collection but OP swab for PCR collected by test centre personnel)</p> <p>Transport media: none</p> <p>Sample storage: none</p> <p>Test operator: presume HCW - states "Personnel from the private company Copenhagen Medical A/S"</p> <p>Definition of test positivity: not stated; conducted according to SD BIOSENSOR's instruction</p> <p>Blinding reported: yes; test performed on the site before PCR</p> <p>Timing of samples: no details</p>
Target condition and reference standard(s)	<p>Reference standard: PCR performed using Luna Universal Probe One-step RT-qPCR kit (NewEngland Biolab); Ct \leq 38 and \geq 10 considered positive</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): E-gene</p> <p>Samples used: OP; eluted in PBS</p> <p>Timing of reference standard: no details; as for index test</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes</p> <p>Uninterpretable results: 97/4908 inconclusive on PCR, leaving 4811 samples for inclusion</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): the reasons for 97 missing data was due to inconclusive results on PCR (i.e. Ct > 38)</p> <p>Unit of analysis: samples</p>
Comparative	
Notes	<p>Funding: author report no funding was received for this project</p> <p>Publication status: preprint</p> <p>Source: medRxiv</p> <p>Author COI: author report no COI present</p>

Jakobsen 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			

Jakobsen 2021 (Continued)

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

James 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: targeted screening at a medical centre in USA (mainly asymptomatic); all staff providing patient care were required to participate but testing was optional for non-clinical staff)</p> <p>Recruitment: consecutive (all clinical staff included)</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 2339 (152)</p>
Patient characteristics and setting	<p>Setting: primarily screening; dedicated stations within the hospital (mobile teams) or drive-through parking lot stations</p> <p>Location: Arkansas (name of hospital not reported); study conducted by Arkansas Department of Health, author institution includes St Bernards Medical Center</p> <p>Country: USA</p> <p>Dates: 2-9 October 2020</p> <p>Symptoms and severity: 2224 (95%) asymptomatic; 115 (5%) symptomatic. 94 (82%) reported only one symptom and 21 (18%) reported 2–6 symptoms: fever (6%), cough (29%), sore throat (29%), chills (6%), headache (41%), muscle aches (12%), abdominal pain (4%); none reported loss of taste or loss of smell.</p> <p>Demographics: median 37 (range 16–89) years; gender not reported</p> <p>Exposure history: no details</p>
Index tests	<p>Test name: BinaxNOW COVID-19 Ag Card tests (BinaxNOW)</p> <p>Manufacturer: Abbott Diagnostics, Scarborough, ME</p> <p>Antibody: nucleocapsid protein antigen</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: nasal (nares samples); collected by trained hospital staff in random order for PCR or Ag testing</p> <p>Transport media: none</p>

James 2021 (Continued)

	Sample storage: none Test operator: trained laboratory employees of hospital X Definition of test positivity: not stated Blinding reported: yes; performed on site before RT-PCR Timing of samples: not stated for symptomatic
Target condition and reference standard(s)	Reference standard: RT- PCR using PerkinElmer SARS-CoV-2 real-time RT-PCR assay (PerkinElmer, Waltham, MA); Ct < 42 considered positive Definition of non-COVID cases: as for cases; single negative Genetic target(s): N or Orf1 Samples used: nasal (nares) swab in VTM or saline Timing of reference standard: not stated Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swab All participants received same reference standard: yes Missing data: none Uninterpretable results: none Indeterminate results (index test): none (all paired samples were successfully tested) Indeterminate results (reference standard): none (all paired samples were successfully tested) Unit of analysis: participant
Comparative	
Notes	Funding: none Publication status: published Source: Infection Control & Hospital Epidemiology Author COI: one of the authors report COI unrelated to this manuscript. All other authors report 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		

James 2021 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

James 2021 (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Kerneis 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: symptomatic patients invited for testing (i.e. temperature > 37.8 °C or chills, cough, rhinorrhoea, muscle pain, loss of smell or taste, unusual persistent headaches or severe asthenia), symptomatic contacts of confirmed cases, asymptomatic contacts of confirmed cases (after 7 days self-isolation) and any other asymptomatic individuals wishing to be tested</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 1452 (129)</p>
Patient characteristics and setting	<p>Setting: COVID-19 community testing centres</p> <p>Location: 2 community screening centres located in Paris within the COVISAN program (Assistance Publique-Hôpitaux de Paris, APHP)</p> <p>Country: France</p> <p>Dates: 19 October-18 December 2020</p> <p>Symptoms and severity: 571 (39%) symptomatic, 409 with 1-3 symptoms: cough: 292/1451 (20%); headaches: 257/1451 (18%); rhinorrhoea: 202/1451 (14%); asthenia: 198/1451 (14%); muscle pain: 177/1451 (12%); fever: 163/1451 (11%); diarrhoea: 85/1451 (6%); chills: 69/1451 (5%); anosmia: 62/1451 (4%); shortness of breath: 53/1451 (4%); chest pain: 52/1451 (4%)</p> <p>Demographics: med age (IQR): 36 (26-50); 122 (8%) children Sex: 755/1451 (52%) female</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag test</p> <p>Manufacturer: SD Biosensor, Chuncheongbuk-do, Republic of Korea</p> <p>Antibody: N antigen</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: NP second nostril (collected by trained nurses)</p> <p>Transport media: none used</p> <p>Sample storage: no storage (immediate testing)</p> <p>Test operator: not reported</p> <p>Definition of test positivity: according to manufacturer</p>

Kerneis 2021 (Continued)

	Blinding reported: presumed (based on timing) Timing of samples: med days pso (IQR): 3 (IQR 2-4) Asymptomatic time from last contact 7 (IQR 1-7)
Target condition and reference standard(s)	Reference standard: RT-PCR; TaqPath COVID 19 CE IVD RT PCR Kit (Thermo Fisher Scientific, Coutaboeuf, France) Considered positive if ≥ 1 gene detected; sensitivity analysis for ≥ 2 targets present Definition of non-COVID cases: as for cases Genetic target(s): ORF1ab, N and S-genes Samples used: NP first nostril Timing of reference standard: as for index test Blinded to index test: yes; interpretation "carried out blind of the result of the others (test and of the participant's clinical data)" Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneously All participants received same reference standard: yes Missing data: yes Of 1451 participants who provided samples, 1117 underwent Ag tests (Appendix Figure 1). Reason for missing data not reported Of 1117 tested: 2 technical failures (on Ag test) 6 additional missing results, reason not reported Uninterpretable results: not reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: French Ministry of Health and the Assistance Publique-Hôpitaux de Paris Foundation Publication status: preprint (not peer reviewed) Source: medRxiv Author COI: no COI statement reported, but states "The funding sources had no role in the study's design, conduct and reporting."

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		

Keineis 2021 (Continued)

Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kerneis 2021 (Continued)

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Kilic 2021
Study characteristics

Patient Sampling

Single-group study to estimate sensitivity and specificity: symptomatic patients meeting pre-set criteria for Ag and RT-PCR testing (COVID-19 exposure and ≤ 5 days pso, including fever/flu-like symptoms, unexplained shortness of breath, or new loss of taste)

Recruitment: consecutive; based on all patients meeting criteria for testing

Prospective or retrospective: prospective

Sample size (cases): 1384 (116)

Patient characteristics and setting

Setting: not stated; 'patients receiving care at our hospital system' - likely mixed settings. (www.wakehealth.edu/Find-A-Provider)

Location: author institution: Wake Forest School of Medicine, Winston-Salem, NC

Country: USA

Dates: 20 October-3 December 2020

Symptoms and severity: all symptomatic

Demographics: median age 46.8 years (range 1-98 years), 800 (57.8%) female

Exposure history: seems all had COVID-19 exposure

Index tests

Test name: BD Veritor

Manufacturer: Becton Dickinson, Sparks, Maryland, USA

Antibody: nucleocapsid

Ag target: not stated

Test method: chromatographic

Samples used: nasal samples collected using flocked swabs according to the manufacturer IFU (IFU describes AN collection method)

Transport media: none required

Sample storage: tested at the site of collection within 1 h of collection

Test operator: not stated; presume on-site HCW

Kilic 2021 (Continued)

Definition of test positivity: BD Veritor Analyzer used; no further detail

Blinding reported: yes; performed on site before PCR

Timing of samples: ≤ 5 days from symptom onset

Target condition and reference standard(s)	Reference standard: RT-PCR; Simplexa Covid-19 Direct EUA RT-PCR (Diasorin Molecular LLC, Cypress, CA, USA) Median threshold cycle (Ct) values < 40 (for one or both targets) were reported as positive for SARS-CoV-2 Definition of non-COVID cases: as for cases (single -ve PCR) Genetic target(s): S gene and ORF1ab genes Samples used: NP in VTM; paired Timing of reference standard: same as for index Blinded to index test: not stated Incorporated index test: no
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Flow and timing	Time interval between index and reference tests: paired swab; simultaneous All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
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Comparative

Notes	Funding: not stated Publication status: accepted manuscript posted online Source: Journal of Clinical Microbiology Author COI: authors report no COI present
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Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Yes
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Was a case-control design avoided?	Yes
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Did the study avoid inappropriate inclusions?	Yes
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Could the selection of patients have introduced bias?	Low risk
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Kilic 2021 (Continued)

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Kohmer 2021 [A]

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: individuals from shared living facilities for screening purposes regardless of their clinical symptoms (n = 100)</p> <p>Recruitment: unclear (anonymized clinical samples)</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 100 (74)</p>
Patient characteristics and setting	<p>Setting: community</p> <p>Location: shared living facilities, Frankfurt (Institute for Medical Virology, University Hospital, Goethe University Frankfurt)</p> <p>Country: Germany</p> <p>Dates: November 2020 (2 weeks)</p> <p>Symptoms and severity: not stated</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name:</p> <p>[A] RIDA QUICK SARS-CoV-2 Antigen [B] SARS-CoV-2 Rapid Antigen Test [C] NADAL COVID-19 Ag Test (test cassette) [D] SARS-CoV-2 Ag Test on the LumiraDx Platform</p> <p>Manufacturer: [A] R-Biopharm AG, Darmstadt, Germany [B] Roche Diagnostics GmbH, Mannheim, Germany [C] Nal von Minden GmbH, Regensburg, Germany [D] LumiraDx GmbH, Cologne, Germany</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method:</p> <p>[A], [B], [C] not stated [D] immunofluorescence assay</p> <p>Samples used: NP</p> <p>Transport media: PBS</p> <p>Sample storage: sample storage not stated; tested within 24 h after collection</p> <p>Test operator: not stated</p> <p>Definition of test positivity: for [A], [B], [C] the results were read visually and documented by 3 different individuals, and the majority consensus was chosen as the final test result Not stated for [D] (IFU indicates that a reader device is required)</p> <p>Blinding reported: unclear; parallel testing</p>

Kohmer 2021 [A] (Continued)

	Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR; Cobas 6800 system (Roche Diagnostics International AG, Rotkreuz, Switzerland) system Culture also undertaken for all samples positive on at least 1 genetic target Definition of non-COVID cases: as for cases; single negative PCR Genetic target(s): ORF1 and E-gene; considered positive if ORF1 detected Samples used: NP swab in PBS (same as for index test) Timing of reference standard: not stated Blinded to index test: unclear; parallel testing Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same swab All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: no external funding Publication status: published Source: Journal of Clinical Medicine Author COI: the authors report 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 inclusions?	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

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kohmer 2021 [A] (Continued)

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Kohmer 2021 [B]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] RIDA QUICK SARS-CoV-2 Antigen [B] SARS-CoV-2 Rapid Antigen Test [C] NADAL COVID-19 Ag Test (test cassette) [D] SARS-CoV-2 Ag Test on the LumiraDx Platform</p> <p>Manufacturer:</p> <p>[A] R-Biopharm AG, Darmstadt, Germany [B] Roche Diagnostics GmbH, Mannheim, Germany [C] Nal von Minden GmbH, Regensburg, Germany [D] LumiraDx GmbH, Cologne, Germany</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: [A], [B], [C] not stated [D] immunofluorescence assay</p> <p>Samples used: NP</p> <p>Transport media: PBS</p> <p>Sample storage: sample storage not stated; tested within 24 h after collection</p> <p>Test operator: not stated</p> <p>Definition of test positivity: for [A], [B], [C] the results were read visually and documented by 3 different individuals, and the majority consensus was chosen as the final test result; Not stated for [D] (IFU indicates that a reader device is required)</p> <p>Blinding reported: unclear; parallel testing</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.

Kohmer 2021 [C]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kohmer 2021 [C] (Continued)

Patient characteristics and setting Comparative study of 4 Ag tests; [Kohmer 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Test name:

[A] RIDA QUICK SARS-CoV-2 Antigen
 [B] SARS-CoV-2 Rapid Antigen Test
[C] NADAL COVID-19 Ag Test (test cassette)
 [D] SARS-CoV-2 Ag Test on the LumiraDx Platform

Manufacturer:

[A] R-Biopharm AG, Darmstadt, Germany
 [B] Roche Diagnostics GmbH, Mannheim, Germany
[C] Nal von Minden GmbH, Regensburg, Germany
 [D] LumiraDx GmbH, Cologne, Germany

Antibody: not stated

Ag target: not stated

Test method: **[A], [B], [C] not stated**
 [D] immunofluorescence assay

Samples used: NP

Transport media: PBS

Sample storage: sample storage not stated; tested within 24 h after collection

Test operator: not stated

Definition of test positivity: for **[A], [B], [C] the results were read visually and documented by 3 different individuals, and the majority consensus was chosen as the final test result;**
 Not stated for [D] (IFU indicates that a reader device is required)

Blinding reported: unclear; parallel testing

Timing of samples: not stated

Target condition and reference standard(s) Comparative study of 4 Ag tests; [Kohmer 2021 \[A\]](#) reports full study characteristics and QUADAS.

Flow and timing Comparative study of 4 Ag tests; [Kohmer 2021 \[A\]](#) reports full study characteristics and QUADAS.

Comparative

Notes Comparative study of 4 Ag tests; [Kohmer 2021 \[A\]](#) reports full study characteristics and QUADAS.

Kohmer 2021 [D]
Study characteristics

Patient Sampling Comparative study of 4 Ag tests; [Kohmer 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 4 Ag tests; [Kohmer 2021 \[A\]](#) reports full study characteristics and QUADAS.

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kohmer 2021 [D] (Continued)

Index tests	Test name: [A] RIDAQUICK SARS-CoV-2 Antigen [B] SARS-CoV-2 Rapid Antigen Test [C] NADAL COVID-19 Ag Test (test cassette) [D] SARS-CoV-2 Ag Test on the LumiraDx Platform Manufacturer: [A] R-Biopharm AG, Darmstadt, Germany [B] Roche Diagnostics GmbH, Mannheim, Germany [C] Nal von Minden GmbH, Regensburg, Germany [D] LumiraDx GmbH, Cologne, Germany Antibody: not stated Ag target: not stated Test method: [A], [B], [C] not stated [D] immunofluorescence assay Samples used: NP Transport media: PBS Sample storage: sample storage not stated; tested within 24 h after collection Test operator: not stated Definition of test positivity: for [A], [B], [C] the results were read visually and documented by 3 different individuals, and the majority consensus was chosen as the final test result; Not stated for [D] (IFU indicates that a reader device is required) Blinding reported: unclear; parallel testing Timing of samples: not stated
Target condition and reference standard(s)	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Kohmer 2021 [A] reports full study characteristics and QUADAS.

Kriemler 2021
Study characteristics

Patient Sampling	A single-group study (nested in the Ciao Corona Cohort study) to estimate sensitivity and specificity: children (n = 641) and teachers (n = 66) attending primary or secondary schools over a 1-week period and tested at least once (T1 and or T2) (n = 707). Schools were selected based on high incidence areas; children were required to be kept at home if they were sick beyond very mild symptoms such as runny nose or mild cough. Recruitment: consecutive; all participating children and teachers got the tests
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Kriemler 2021 (Continued)

	<p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 641 children and adolescents and 66 teachers tested at T1 and or T2; children provided 1170 samples (1 PCR+) (567 at T1 and 602 at T2), total N not reported for teachers (0 PCR+). Data obtained from study authors: 117 samples from teachers (62 at T1 and 57 at T2)</p>
Patient characteristics and setting	<p>Setting: screening in schools</p> <p>Location: schools in the city of Zurich and 1 school of each of 4 adjacent districts Author institution: Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich,</p> <p>Country: Switzerland</p> <p>Dates: 1-11 December 2020</p> <p>Symptoms and severity: at T1, 198/567 (35%) children and 5/66 (8%) teachers reported mild symptoms (runny nose, headache, cough stomach upset, etc) during the previous 5 days before testing. Symptoms of week 1 (T1) and 2 (T2) reported not to differ significantly</p> <p>Demographics: children and adolescents: age range 10-19 years; 370 (58%) female children and adolescents; 46 (70%) female teachers</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test</p> <p>Manufacturer: SD Biosensor/Roche, Switzerland</p> <p>Antibody: none stated</p> <p>Ag target: none stated</p> <p>Test method: CGIA</p> <p>Samples used: buccal swab taken with closed mouth over 1 min (study staff members) (2 swabs were held closely together so that they were exposed to the same location of the enoral space. Swabbing of the mucosal membrane was done in the whole enoral space with some pressure application to make sure to have some cells contained in the swab)</p> <p>Transport media: none required; direct swab</p> <p>Sample storage: none required; direct swab</p> <p>Test operator: study staff member (experienced in RDT testing)</p> <p>Definition of test positivity: visual Judged by 2 study team members (experienced in RDT testing) in agreement as positive or negative and blinded to reported symptoms</p> <p>Blinding reported: yes; performed on the site before PCR</p> <p>Timing of samples: essentially asymptomatic testing although some symptoms (runny nose, cough headache etc) reported</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR (Analytica, Zurich, Switzerland); performed using the CE-IVD-marked Allplex™ SARS-CoV-2 Assay (Seegene Inc, Seoul, Republic of Korea)</p> <p>Definition of non-COVID cases: same as for cases</p> <p>Genetic target(s): N, S, RdRP and E-gene</p> <p>Samples used: buccal swab (taken with closed mouth over 1 min)</p>

Kriemler 2021 (Continued)

Timing of reference standard: as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: parallel buccal swab

All participants received same reference standard: yes

Missing data: yes; participants were not all tested at T1 (88% of children tested) and T2 (94%)

Uninterpretable results: none reported

Indeterminate results (index test): none reported; judged by 2 study team members (experienced in RDT testing) in agreement as positive or negative

Indeterminate results (reference standard): none reported

Unit of analysis: participants and samples

Comparative

Notes

Funding: "this study is funded by fundraising of SSPH+ that includes funds of the Swiss Federal Office of Public Health and private funders, by Cantons of Switzerland, by institutional funds of the Universities and by the University of Zurich Foundation and the Federal Office of Public Health"

Publication status: published

Source: Frontiers in Pediatrics

Author COI: authors report 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kriemler 2021 (Continued)

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

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

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kriemler 2021 (Continued)

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Kruger 2021
Study characteristics

Patient Sampling Single-group multi-centre study to estimate sensitivity and specificity: adults at risk of SARS-CoV-2 infection based on reported symptoms or recent contact with a confirmed case (according to the criteria of the national health authority)
 Group [1]: Heidelberg
 Group [2]: Berlin
 (Group [1] and group [2] are reported as subgroups)
 Recruitment: not reported; known to be consecutive recruitment
 Prospective or retrospective: prospectively
 Sample size (cases): 767 (146)

Patient characteristics and setting Setting: COVID-19 testing site
 [1] Drive-in testing site
 [2] Clinical ambulatory testing facility
 Location: [1]: Heidelberg (authors' institutions include Heidelberg University Hospital)
 [2]: Berlin (authors' institutions include Berlin Institute of Health)
 Country: Germany
 Dates: 2 November- 4 December 2020
 Symptoms and severity: 486 (64%) symptomatic on day of testing; 90 (19%) fever, 247 (52%) cough, 242 (50%) sore throat, 297 (62%) fatigue
 Raw symptom data in a supplementary table
www.medrxiv.org/content/10.1101/2021.03.02.21252430v1.supplementary-material (Section E, Table 1, p19)
 Demographics: average age: 38.5 years (SD 14.2)
 Sex: (52%) female
 Exposure history: all asymptomatic participants (36%) were recent high-risk contacts

Index tests Test name: LumiraDx SARS-CoV Ag test
 Manufacturer: LumiraDx Limited, London, UK
 Antibody: nucleocapsid protein of SARS-CoV-2
 Ag target: not reported
 Test method: FIA; microfluidic immunofluorescence assay
 Samples used: NMT (by participants themselves with HCW providing instructions, supervision and corrections)

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kruger 2021 (Continued)

Sample collection was performed with Dryswab Standard Tip Rayon (Medical Wire & Equipment, Corsham, England)

Transport media: none used

Sample storage: no storage

Test operator: laboratory personnel in dedicated workspace (no further details reported)

Definition of test positivity: according to manufacturer; digital touch screen readout of positive, negative or error (error results re-tested using same extraction vial with a new test strip)

Blinding reported: yes

Timing of samples: average symptom duration of 3.9 days (SD 3.2)
423/472 (90%) of symptomatic patients reported onset of symptoms within the prior 7 days

Target condition and reference standard(s)

Reference standard: RT-PCR

[A] In Heidelberg: Allplex SARS-CoV-2 assay (Seegene, Seoul, South Korea)

[B] In Berlin: Cobas SARS CoV-2 assay on the Cobas 6800 or 8800 system (Roche, Pleasanton, CA, USA)

OR

SARS CoV-2 assay from TIB Molbiol (Berlin, Germany)

Assays interpreted according to manufacturer IFU

Conversion of CT values into viral load was based on calibrated RT-PCR testing with quantified SARS-CoV-2 in vitro transcripts.

Definition of non-COVID cases: as for cases; single negative

Genetic target(s): E-gene

Samples used:

[A] in Heidelberg: NP

[B] in Berlin: combined NP/OP (OP alone used only if clinical contraindications for NP sampling)

RT-PCR samples were collected by HCWs using the IMPROSWAB (Guangzhou Improve Medical Instruments Co., Ltd., Guangzhou, China)

Timing of reference standard: same as for index test

Blinded to index test: yes; stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired samples; reference swab obtained after index test swab

All participants received same reference standard: yes

Missing data: yes; 2 refused NMT swab and 4 had invalid RT-PCR results

Uninterpretable results: 7 samples gave error message on LumiraDx device; repeat testing yielded valid results and inclusion in the analysis

Indeterminate results (index test): not reported

Indeterminate results (reference standard): 4 invalid RT-PCR results excluded

Unit of analysis: participant

Comparative

Notes

Funding: "the study was supported by the Ministry of Science, Research and Arts of the State of Baden- Wuerttemberg, Germany and internal funds from the Heidelberg University Hospital and

Kruger 2021 (Continued)

University Hospital Charité -Universitätsmedizin Berlin as well as grants from UK Department of International Development (DFID, recently replaced by FCMO), grants from World Health Organization (WHO), grants from Unitaid to Foundation of New Diagnostics (FIND). The testing devices and all components were provided by the manufacturer. T.C.J. is in part funded through NIAID-NIH CEIRS."

Publication status: preprint (not peer reviewed)

Source: medRxiv

Author COI: none reported; "The manufacturer and funders had no input into the study protocol, the analysis or interpretation of the results."

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			

Kruger 2021 (Continued)

Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Low risk

Kruttgen 2021
Study characteristics

Patient Sampling	2-group study to estimate sensitivity and specificity [1] patients previously tested positive by RT-PCR (n = 75) [2] patients previously tested negative by RT-PCR (n = 75)
	Recruitment: unclear
	Prospective or retrospective: retrospective
	Sample size (cases): 150 (75)

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kruttgen 2021 (Continued)

Patient characteristics and setting	Setting: not stated; SARS-CoV-2-negative were reported as hospital inpatient Location: RWTH Aachen University hospital Country: Germany Dates: not stated Symptoms and severity: not stated Demographics: not stated Exposure history: not stated
Index tests	Test name: SARS-CoV-2 Rapid Antigen Test Manufacturer: Roche, Switzerland Antibody: not stated Ag target: not stated Test method: not stated Samples used: NP Transport media: swab transport medium used Sample storage: not stated; states no intermittent freeze-thaw cycle so presume no frozen storage Test operator: laboratory staff Definition of test positivity: visual; test and control lines Blinding reported: unclear Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR: Real Star SARS-CoV-2 RT PCR Kit (Altona, Germany) Definition of non-COVID cases: same as for cases Genetic target(s): not stated Samples used: NP Timing of reference standard: not stated Blinded to index test: yes (conducted before index test) Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same swab All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported

Kruttgen 2021 (Continued)

Unit of analysis: participant

Comparative

Notes

Funding: none

Publication status: published

Source: Journal of Virological Methods

Author COI: author report 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		

Kruttgen 2021 (Continued)

Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

L'Huillier 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: children (0-16 years old) meeting eligibility criteria for RT-PCR testing: 1) symptoms suggestive of COVID infection according to local governmental testing criteria, and for asymptomatic children either 2) contact with a laboratory-confirmed COVID infected person and 3) pre-travel testing</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 885 (119); 60 excluded a priori</p>
Patient characteristics and setting	<p>Setting: paediatric COVID-19 testing centre</p> <p>Location: Geneva University Hospitals (HUG)</p> <p>Country: Switzerland</p> <p>Dates: 10 November 2020-26 March 2021</p> <p>Symptoms and severity: 533 (65%) symptomatic: headache (58%), nasal discharge (55%), cough (44%), fatigue (44%), dysphagia (41%), fever (30%), abdominal pain (20%), myalgia (16%), diarrhoea (15%); shortness of breath (8%), anosmia (7%)</p> <p>Asymptomatic: 289 (35%)</p> <p>Demographics: all children; median age 12.1 (IQR 9.4-14.5); 266 (50%) female</p> <p>Exposure history: not stated; contacts with COVID cases</p>
Index tests	<p>Test name: PanbioTM-COVID-19 Ag Rapid Test Device</p> <p>Manufacturer: Abbott Rapid Diagnostics, USA</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not stated</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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L'Huillier 2021 (Continued)

	<p>Test method: CGIA</p> <p>Samples used: NP from the contralateral or ipsilateral nostril (collected by trained nurses)</p> <p>Transport media: none used</p> <p>Sample storage: none required</p> <p>Test operator: 2 members of the study team; blinded to each other and to clinical presentation</p> <p>Definition of test positivity: visual; control and test line Any discrepant result was considered positive when any of the above-mentioned reader set a positive diagnosis</p> <p>Blinding reported: yes (performed before PCR)</p> <p>Timing of samples: for symptomatic patients samples were taken at median 2 days pso (IQR 1-3)</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR: either</p> <ol style="list-style-type: none"> 1. Cobas SARS-CoV-2 assay (Cobas SARS-CoV-2 Test, Cobas 6800, Roche, Switzerland) or 2. Nimbus RT-PCR assay <p>Definition of non-COVID cases: same as for cases (single -ve PCR)</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP (flocked swab in 3 mL VTM)</p> <p>Timing of reference standard: for symptomatic patients samples were taken at median 2 days pso (IQR 1-3)</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous; paired</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes; 63/885 (7%) excluded from analysis 1 excluded a priori (did not meet inclusion criteria), 1 refused RT-PCR, and 58 refused Ag test (n = 58); 3 excluded after testing</p> <p>Uninterpretable results: 2 Ag test result not reported and 1 Ag test result invalid Among the 822 Ag tests</p> <p>Indeterminate results (index test): none; only 1 discrepant between readers (considered +ve)</p> <p>Indeterminate results (reference standard)</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: supported by the Geneva Centre for Emerging Viral Diseases</p> <p>Publication status: preprint</p> <p>Source: medRxiv preprint</p>

L'Huillier 2021 (Continued)

Author COI: the authors declare 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

L'Huillier 2021 (Continued)

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

High risk

Lambert-Niclot 2020
Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity: samples submitted for RT-PCR testing (n = 138) Recruitment: not stated Prospective or retrospective: unclear; testing conducted prospectively Number of samples (samples with confirmed SARS-CoV-2): 138 (94)
Patient characteristics and setting	Setting: not stated Location: samples collected from virology laboratories of 3 university hospital groups from Assistance-Publique-Hôpitaux de Paris (APHP), (Saint-Antoine-Tenon-Trousseau, Saint-Louis-Lariboisière and Kremlin Bicêtre-Paul Brousse) Country: France Dates: 1-15 April 2020 Symptoms and severity: not stated Demographics: not stated Exposure history: not stated
Index tests	Test name: COVID-19 Ag Respi-Strip CORIS (no product code) Manufacturer: BioConcept, Gembloux, Belgium Ag target: SARS-CoV-2 NP Antibody: monoclonal antibodies

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Lambert-Niclot 2020 (Continued)

	<p>Test method: CGIA</p> <p>Samples used: NP swabs in VTM (collection process not described)</p> <p>Transport media: either of: COPAN UTM 3 mL, Virocult 1 mL, Eswab Amies 1 mL, 4MRT 3 mL, 0.9% NaCl buffer and Cobas ROCHE</p> <p>Sample storage: no cooling or freezing step used</p> <p>Test operator: not stated; presume laboratory staff</p> <p>Definition of test positivity: not stated; as per manufacturer IFU</p> <p>Blinding reported: not stated</p> <p>Timing of samples: not stated; presume on presentation</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR (different kits used including RealStar Altona, Anatolia, Cobas 6800 Roche, Allplex 2019-nCoV Assay Seegene)</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): E gene</p> <p>Samples used: NP swabs (same as for index)</p> <p>Timing of reference standard: within a few hours after collection; time pso not reported</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same sample, both tests conducted within a few hours</p> <p>All participants received same reference standard: yes (different kits)</p> <p>Missing data: none reported</p> <p>Uninterpretable results: 4 samples collected in Cobas VTM gave invalid results and all samples in Cobas medium were excluded</p> <p>Indeterminate results (index test): control lines reported as "barely visible" for 9 positive and 8 negative tests</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: not reported, but samples tested on day of collection so considered to be 1 per participant</p>
Comparative	
Notes	<p>Funding: no funding sources reported</p> <p>Publication status: accepted manuscript</p> <p>Source: Journal of Clinical Microbiology</p> <p>Author COI: no conflict of interest statement reported</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Lambert-Niclot 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 inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Lambert-Niclot 2020 *(Continued)*

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

Lanser 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity alone A group of patients with PCR-confirmed COVID-19 during their hospital stay in different stages of the disease. All patients received Ag test along with RT-PCR (n = 53) 2 patients with negative PCR were excluded due to apparent subsidence of infection</p> <p>Recruitment: unclear</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 53 (100%) included; 51 analysed 2 COVID patients were RT-PCR-ve suggesting an already subsided infection and were excluded from the analysis</p>
Patient characteristics and setting	<p>Setting: hospital inpatient</p> <p>Location: Department of Internal Medicine II, Innsbruck Medical University, Innsbruck</p> <p>Country: Austria</p> <p>Dates: not stated</p> <p>Symptoms and severity: in different stages of the COVID infection</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Panbio COVID-19 Ag Rapid test</p> <p>Manufacturer: Abbott, Chicago, Illinois, USA</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP</p> <p>Transport media: none required</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Lanser 2021 (Continued)

	<p>Sample storage: none required</p> <p>Test operator: not stated; probably HCW</p> <p>Definition of test positivity: not stated; visual</p> <p>Blinding reported: no; conducted before RT-PCR but all had previously confirmed COVID-19</p> <p>Timing of samples: unclear; states "sample taken during their hospital stay in different stages of the disease"</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR using the Cobas analyzer (Roche Diagnostics GmbH, Mannheim, Germany)</p> <p>Definition of non-COVID cases: NA</p> <p>Genetic target(s): Orf1</p> <p>Samples used: NP</p> <p>Timing of reference standard: unclear; states "sample taken during their hospital stay in different stages of the disease"</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes, 2/53 COVID patients were RT-PCR–ve suggesting an already sub-sided infection and were excluded from the analysis</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: none</p> <p>Publication status: published</p> <p>Source: Infection</p> <p>Author COI: the authors declare no conflict of interest</p>

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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Lanser 2021 (Continued)

Did the study avoid inappropriate inclusions?	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?		High
DOMAIN 2: Index Test (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	No	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Did all participants receive a reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Lanser 2021 (Continued)

Could the patient flow have introduced bias?

Low risk

Linares 2020
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity, recruiting at 2 locations: [1] symptomatic patients admitted to ED with clinical suspicion of COVID-19 (n = 135) or asymptomatic patients with history of contact with another COVID-19 patient (n = 17) [2] symptomatic patients (n = 50) or asymptomatic (n = 55) patients attending 1 of 2 primary healthcare centres</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: unclear; appears to be prospective</p>
Patient characteristics and setting	<p>Setting: mixed; ED or primary care</p> <p>Location: Hospital Universitario Príncipe de Asturias, Madrid</p> <p>Country: Spain</p> <p>Dates: 10-15 September</p> <p>Symptoms and severity: 185, 72% symptomatic; 72, 28% asymptomatic ED (n = 135): fever 40, dyspnoea 42, cough 22, headache 14 Primary care (n = 50): fever 14, dyspnoea 1, cough 18, headache 17</p> <p>Demographics: mean age (range): ED 51.5 years (37.0-71.8 years); primary care 39.0 years (25.0-56.0 years) Male: ED 77 (51%), primary care 49 (47%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: PanBio COVID-19 Ag Rapid Test Device (no product code)</p> <p>Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not stated</p> <p>Test method: not stated; qualitative membrane-based immunoassay (immunochromatography)</p> <p>Samples used: NP; HCW obtained</p> <p>Transport media: none reported</p> <p>Sample storage: not stated</p> <p>Test operator: not stated</p> <p>Definition of test positivity: not stated; as per manufacturer IFU</p> <p>Blinding reported: not stated</p> <p>Timing of samples: ED: 2 days pso (IQR? 1-5) PC: 4 days pso (IQR? 2-8)</p>

Linares 2020 (Continued)

Table 3 reports range of 0-27 days pso or post COVID-19 contact, and range of 0-16 days for days pso for symptomatic cases only

Target condition and reference standard(s)	Reference standard: RT-PCR; Allplex SARS-CoV-2 assay (Seegene, Seoul, South Korea); appears to be < 40 Ct threshold Definition of non-COVID cases: as for cases (single -ve) Genetic target(s): not stated Samples used: NP (paired) Timing of reference standard: not stated Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: paired All participants received same reference standard: yes Missing data: none reported however 257 reported in Methods and 255 in Results, no participant flow diagram reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: no funding statement provided Publication status: preprint Source: medRxiv Author COI: no COI statement provided

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 inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	

Linares 2020 (Continued)

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Lindner 2021a [A]

Study characteristics

Patient Sampling	<p>A single-group study to estimate sensitivity and specificity Mainly symptomatic adults at high risk for SARS-CoV-2 infection according to clinical suspicion of COVID-19</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 289 (39)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre</p> <p>Location: ambulatory SARS-CoV-2 testing facility of Charité University Hospital, Berlin (Division of Clinical Tropical Medicine, Center of Infectious Diseases, Heidelberg University Hospital, Heidelberg)</p> <p>Country: Germany</p> <p>Dates: 23 September-14 October 2020</p> <p>Symptoms and severity: on day of testing: 283 (98%) symptomatic; 6 (2%) asymptomatic; average symptom duration 4.4 days (SD 2.7)</p> <p>Demographics: average age 34.7± 11 years; 42.9% female and 19.0% with comorbidities</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea; (also being distributed by Roche)</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: LFA chromatographic</p> <p>Samples used: [A] AN; instructed, self-collected (Verbal instruction was given to insert the swab horizontally 2-3 cm into the nostril and rotate it for 15 s against the nasal walls on each side. Deviations from the instructed technique were recorded.) [B] NP; collected by study physicians</p> <p>Transport media: none required</p> <p>Sample storage: none required</p> <p>Test operator: study physicians</p> <p>Definition of test positivity: visual; presence of control test lines, categorized as negative, weak positive, positive and strong positive Results interpreted by 2 operators, each blinded to the result of the other. The second reader was also blinded to the result from the alternative sampling method</p> <p>Blinding reported: yes; states "Staff performing the Ag-RDTs were blinded to results of PCR tests and vice versa."</p> <p>Timing of samples: average symptom duration 4.4 days (SD 2.7) (range 1-14 days for PCR+ group)</p>

Lindner 2021a [A] (Continued)

Target condition and reference standard(s)	Reference standard: PCR using Roche Cobas SARS-CoV-2 assay (Pleasanton, CA USA) or the SARS-CoV-2 E-gene assay from TibMolbiol (Berlin, Germany) Definition of non-COVID cases: single negative PCR Genetic target(s): E-gene Samples used: OP+NP combined swab Timing of reference standard: as for index test Blinded to index test: yes; states "Staff performing the Ag-RDTs were blinded to results of PCR tests and vice versa." Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous All participants received same reference standard: yes Missing data: yes; 2 excluded as both swabs for the Ag test could not be obtained Uninterpretable results: none reported Indeterminate results (index test): none; "no invalid tests were observed" Indeterminate results (reference standard): none; "no invalid tests were observed" Unit of analysis: participant
Comparative	
Notes	Funding: "supported by FIND, Heidelberg University Hospital and Charité University Hospital internal funds, Ministry of Science, Research and the Arts of Baden-Württemberg, Germany" Publication status: in press (published as in accepted form) Source: European Respiratory Journal Author COI: authors report 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 inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	

Lindner 2021a [A] *(Continued)*

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

Low concern

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Lindner 2021a [A] (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Lindner 2021a [B]
Study characteristics

Patient Sampling	Comparative study of an Ag test on 2 different sample types; Lindner 2021a [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of an Ag test on 2 different sample types; Lindner 2021a [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea; (also being distributed by Roche)</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: LFA Chromatographic</p> <p>Samples used: [A] AN; instructed, self-collected (Verbal instruction was given to insert the swab horizontally 2-3 cm into the nostril and rotate it for 15 seconds against the nasal walls on each side. Deviations from the instructed technique were recorded.)</p> <p>[B] NP; collected by study physicians</p> <p>Transport media: none required</p> <p>Sample storage: none required</p> <p>Test operator: study physicians</p> <p>Definition of test positivity: visual; presence of control test lines, categorized as negative, weak positive, positive and strong positive</p> <p>Results interpreted by 2 operators, each blinded to the result of the other. The second reader was also blinded to the result from the alternative sampling method</p> <p>Blinding reported: yes; States "Staff performing the Ag-RDTs were blinded to results of RT-PCR tests and vice versa."</p> <p>Timing of samples: average symptom duration 4.4 days (SD 2.7) (range 1-14 days for PCR+ group)</p>
Target condition and reference standard(s)	Comparative study of an Ag test on 2 different sample types; Lindner 2021a [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of an Ag test on 2 different sample types; Lindner 2021a [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of an Ag test on 2 different sample types; Lindner 2021a [A] reports full study characteristics and QUADAS.

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Lindner 2021b [A]

Study characteristics

Patient Sampling	<p>A single-group study to estimate sensitivity and specificity 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</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 146 (40)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre</p> <p>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</p> <p>Country: Germany</p> <p>Dates: 30 November-11 December 2020 (Recruitment dates do not overlap either FIND 2021c (DE) [A] (has associated preprint by Lindner et al) or Lindner 2021a [A])</p> <p>Symptoms and severity: 100% symptomatic; mean duration of pso 3.4 days (SD 2.0) 34 (23%) with comorbidities</p> <p>Demographics: mean age 35 years (SD 11.5); 75 (51%) were female</p> <p>Exposure history: included those with reported contact with a confirmed case. No further details</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea; also distributed by Roche</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] NMT (self-collected and interpreted; according to manufacturer IFU) [B] NMT (self-collected, professional interpreted; according to manufacturer IFU) [C] NP (professional collected and interpreted - trained study physician)</p> <p>Transport media: none required</p> <p>Sample storage: none required</p> <p>Test operator: [A] participants tested NMT sample (according to manufacturer IFU); observed without answering questions or providing corrections [B] Participants tested NMT sample; interpretation by study physician [C] Trained study physician tested and interpreted NP sample All professional test interpretation was by 2 study physicians, each blinded to the result of the other and to the participant's interpretation of the self-test. The second reader was also blinded to the corresponding pairs (NMT/NP) of Ag-RDTs belonging to 1 individual.</p> <p>Definition of test positivity: visual The visual read-out of the Ag test band was categorized as negative, weak positive, positive, or strong positive. The participant interpreted the test result as positive, negative, invalid, or don't know.</p>

Lindner 2021b [A] (Continued)

Blinding reported: yes; conducted first

Timing of samples: mean duration of pso 3.4 days (SD 2.0)

Target condition and reference standard(s)

Reference standard: RT-PCR using the Roche Cobas SARS-CoV-2 assay (Pleasanton, CA USA) or the SARS-CoV-2 E-gene assay from TIB Molbiol (Berlin, Germany)

Definition of non-COVID cases: same as cases (single -ve PCR)

Genetic target(s): E gene (Tib Molbiol)

Samples used: combined OP/NP; paired swab

Timing of reference standard: mean duration of pso 3.4 days (SD 2.0)

Blinded to index test: yes; explicitly stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous

All participants received same reference standard: yes

Missing data: yes; 4 excluded (3 participants were excluded as they did not fulfil the minimum language criterion and 1 participant excluded because of lost PCR specimen)

Uninterpretable results: NMT - 1 participant left without reading the test result for nasal sample plus 1 invalid result (buffer spilt and test not repeated)

None reported for NP sample

Indeterminate results (index test): none reported; weak positives considered positive

Indeterminate results (reference standard): none reported

Comparative

Notes

Funding: "study was supported by Foundation of Innovative New Diagnostics (FIND), Charité University Hospital internal funds, as well as a grant of the Ministry of Science, Research and the Arts of Baden-Württemberg, Germany"

Publication status: preprint

Source: medRxiv

Author COI: one author reports grants from FIND and Ministry of Science, Research and Culture, State of Baden Wuerttemberg, Germany. Another author reports grants from DFID (recently replaced byFCMO), 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 inclusions?	Yes		

Lindner 2021b [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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Lindner 2021b [A] *(Continued)*

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

Lindner 2021b [B]
Study characteristics

Patient Sampling	Comparative study of 3 different sample types (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea; also distributed by Roche</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] NMT (self-collected and interpreted; according to manufacturer IFU) [B] NMT (self-collected, professional interpreted; according to manufacturer IFU) [C] NP (professional collected and interpreted - trained study physician)</p> <p>Transport media: none required</p> <p>Sample storage: none required</p> <p>Test operator: [A] participants tested NMT sample (according to manufacturer IFU); observed without answering questions or providing corrections [B] Participants tested NMT sample; interpretation by study physician [C] Trained study physician tested and interpreted NP sample All professional test interpretation was by 2 study physicians, each blinded to the result of the other and to the participant's interpretation of the self-test. The second reader was also blinded to the corresponding pairs (NMT/NP) of Ag-RDTs belonging to 1 individual.</p> <p>Definition of test positivity: visual The visual read-out of the Ag test band was categorized as negative, weak positive, positive, or strong positive. The participant interpreted the test result as positive, negative, invalid, or don't know.</p> <p>Blinding reported: yes; conducted first</p>

Lindner 2021b [B] *(Continued)*

Timing of samples: mean duration of pso 3.4 days (SD 2.0)

Target condition and reference standard(s)	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.

Lindner 2021b [C]
Study characteristics

Patient Sampling	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea; also distributed by Roche</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: [A] NMT (self-collected and interpreted; according to manufacturer IFU) [B] NMT (self-collected, professional interpreted; according to manufacturer IFU) [C] NP (professional collected and interpreted - trained study physician)</p> <p>Transport media: none required</p> <p>Sample storage: none required</p> <p>Test operator: [A] participants tested NMT sample (according to manufacturer IFU); observed without answering questions or providing corrections [B] Participants tested NMT sample; interpretation by study physician [C] Trained study physician tested and interpreted NP sample All professional test interpretation was by 2 study physicians, each blinded to the result of the other and to the participant's interpretation of the self-test. The second reader was also blinded to the corresponding pairs (NMT/NP) of Ag-RDTs belonging to 1 individual.</p> <p>Definition of test positivity: visual The visual read-out of the Ag test band was categorized as negative, weak positive, positive, or strong positive. The participant interpreted the test result as positive, negative, invalid, or don't know.</p> <p>Blinding reported: yes; conducted first</p> <p>Timing of samples: mean duration of pso 3.4 days (SD 2.0)</p>

Lindner 2021b [C] (Continued)

Target condition and reference standard(s)	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 different sample type (self versus professional); Lindner 2021b [A] details full study characteristics and QUADAS.

Liotti 2021
Study characteristics

Patient Sampling	<p>Unclear design estimating sensitivity and specificity; residual samples selected from 1 of 2 virology laboratories at 2 COVID-19 reference hospitals:</p> <p>[1] RT-PCR+ve for SARS-CoV-2 (n = 104)</p> <p>[2] RT-PCR-ve for SARS-CoV-2 (n = 255)</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: retrospective</p>
Patient characteristics and setting	<p>Setting: unclear; laboratory samples</p> <p>Location: from study authors' institutions: Fondazione Policlinico Universitario A. Gemelli IRCCS, and Istituto Nazionale per le Malattie Infettive (INMI) Lazzaro Spallanzani IRCCS, Rome</p> <p>Country: Italy</p> <p>Dates: not stated</p> <p>Symptoms and severity: not stated</p> <p>Of SARS-CoV-2-positive samples, 21, 20% high viral load (< 25 Ct), 83, 80% low viral load (≥ 25) [28, 27% with Ct ≥ 35]</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: STANDARD F COVID-19 Ag FIA (no product codes reported)</p> <p>Manufacturer: SD Biosensor (Suwon, South Korea)</p> <p>Antibody: NP</p> <p>Ag target: monoclonal anti-SARS-CoV-2 antibody</p> <p>Test method: FIA</p> <p>Samples used: NP; collection not reported</p> <p>Transport media: not stated</p> <p>Sample storage: performed within 24 h after collection on samples kept at 4 °C until testing</p>

Liotti 2021 (Continued)

	Test operator: not stated; presume laboratory staff Definition of test positivity: as per manufacturer IFU Blinding reported: not stated Timing of samples: not reported
Target condition and reference standard(s)	Reference standard: RT-PCR (1 of 4 assays); Altona Diagnostics RealStar SARS-CoV-2 RT-PCR, the Seegene Allplex 2019-nCoV, the DiaSorin SimplexaCOVID-19 Direct or the Roche Diagnostics Cobas SARS-CoV-2 test Definition of non-COVID cases: as for cases (single negative) Genetic target(s): not stated Samples used: NP (same as index) Timing of reference standard: not stated Blinded to index test: yes (performed first) Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous (same swab) All participants received same reference standard: yes Missing data: none reported, no participant flow diagram reported Uninterpretable results: none reported Indeterminate results (index test): none reported FP results were re-tested with Ag assay, 3 of 4 remained positive (all blood contaminated) Indeterminate results (reference standard): none reported Unit of analysis: not stated
Comparative	
Notes	Funding: "study supported by funds to the Istituto Nazionale per le Malattie Infettive (INMI) Lazzaro Spallanzani IRCCS, Rome, Italy, from the Ministero della Salute (Ricerca Corrente, linea 1; COVID- 2020-12371817), the European Commission e Horizon 2020 (EU project 101003544 e CoNVat; EU project 101003551 e EXSCALATE4CoV; EU project 12371675 e EXCALATE4CoV; EU project 101005075 e KRONO) and the European Virus Archive e GLOBAL (grants no. 653316 and no. 871029)." Publication status: published letter Source: Clinical Microbiology and Infection Author COI: all authors report no relevant 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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Liotti 2021 (Continued)

Was a case-control design avoided?	Unclear
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)	
DOMAIN 3: Reference Standard	
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes

Liotti 2021 (Continued)

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Love 2021
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity</p> <p>Asymptomatic adult contacts (> 18 years) of a confirmed COVID-19 case (in previous 48 h) identified via NHS Test and Trace and invited to participate. Negative LFD results allowed exemption from self-isolation for a 24-h period until next LFD.</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Exclusions included exposure to confirmed case > 48 h (n = 68) or late or non-arrival of testing kits (n = 27)</p> <p>Sample size (cases): 882/1760 (50.1%) contacts agreed to participate; 812/882 were sent a testing kit. In-study PCR results available for 346 contacts (64 PCR+)</p>
Patient characteristics and setting	<p>Setting: contacts; self-testing</p> <p>Location: UK</p> <p>Country: UK</p> <p>Dates: 11-23 December 2020 and 4-12 January 2021</p> <p>Symptoms and severity: 55/346 self-reported symptoms in prior 14 d (15.9%)</p> <p>Demographics: based on 882 consenting - mean age 42 years (18-82 years); 430, 49% male; 731 (89%) white, 33 Asian, 19 black, 25 mixed race, 14 other</p> <p>Exposure history: all confirmed contacts</p>
Index tests	<p>Test: Innova LFD antigen test</p> <p>Manufacturer: Innova Medical Group</p> <p>Ag target: not reported</p> <p>Test method: CGIA</p> <p>Samples used: nasal (self-collected)</p> <p>Test operator: self-tested. Convenience sample of 1221 LFD images were checked by 2 independent reviewers; 97.1% of images were concordant (n = 1187; 1132 negative and 55 positive results)</p>

Love 2021 (Continued)

	Definition of test positivity: visual; used according to the manufacturer IFU Blinding reported: yes (performed before reference standard) Timing of samples: all asymptomatic on recruitment and tested during the first 7-days post-exposure
Target condition and reference standard(s)	Reference standard: LDT at PHE-accredited laboratory; NHS Test and Trace records also examined to identify confirmatory testing through an approved alternative route Definition of non-COVID cases: single -ve PCR Genetic target(s): ORF1ab, E gene Samples used: nasal (self-collected) Timing of reference standard: median time between reporting a positive LFD result and receipt of PCR swab in the laboratory was 2 days (IQR 1-3 days). Median time between last negative LFD result and the swab being received at the lab was 3 days (IQR 2-5 days). Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: any interval allowed; LFD-negative participants only had PCR at end of study period All participants received same reference standard: yes (if limit to within-study PCR testing) Missing data: 570/812 who were sent a testing kit returned at least 1 LFD result (total of 2946 results); results excluded if duplicate entries (n = 225), blank entries (n = 189), no identifiers (n = 27), or reporting by non-eligible participant (n = 13) Uninterpretable results: invalid results mentioned but not quantified (grouped with negatives) Indeterminate results (index test): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "DR and IO acknowledge support from the NIHR Health Protection Research Unit in Behavioural Science and Evaluation at University of Bristol. SH is supported by the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Healthcare Associated Infections and Antimicrobial Resistance at the University of Oxford in partnership with Public Health England (PHE)." Publication status: preprint Source: medRxiv Author COI: no conflicts of interest statement provided but is PHE (public) funded study

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		

Love 2021 (Continued)

Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		

Love 2021 (Continued)

Was there an appropriate interval between index test and reference standard?	No
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

Masia 2021 [A]
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: symptomatic with COVID-19 signs/symptoms or asymptomatic contacts attending the primary care centres (n = 690 (76%) NP sample), and a majority of symptomatic patients presenting to the ED (n = 233 (25%) NP sample)</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases):</p> <p>[A] NP: 904 (195) [B] Nasal: 659 (132) [C] Saliva: 611 (121)</p>
Patient characteristics and setting	<p>Setting: mixed: primary care centres and an ED</p> <p>Location: Alicante, Spain (Universidad Miguel Hernández)</p> <p>Country: Spain</p> <p>Dates: 15 September-29 October 2020</p> <p>Symptoms and severity: 617 (68%) symptomatic; 296 (32%) asymptomatic Median (Q1-Q3) pso days: 3 (2-5) days Most frequent symptoms were cough (50%), fever (47%), sore throat (32%), and nasal congestion (31%) Median (Q1-Q3) Ct: 24 (16-30) 22 (16-29) in symptomatic and 28 (21-32) in asymptomatic; and 21 (15-27) in patients ≥ 50 years and 26 (18-31) in < 50 years.</p> <p>Demographics: median (Q1-Q3) age 40.6 (23.0-55.6) years; 423 (46%) male</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Panbio COVID-19 Ag RTD</p> <p>Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany</p>

Masia 2021 [A] (Continued)

Antibody: nucleocapsid

Ag target: not reported

Test method: CGIA

Samples used at primary care centres:
[A] NP swabs (1 swab for each nostril) (qualified nurse)
 [B] nasal swab (from 1 nostril) (qualified nurse)
 [C] saliva (patients repeatedly spit up to a minimum of 1 mL of saliva into a 100-mL sterile empty container) (self-collected)

Samples used at the ED:
 [A] NP swab (1 swab for each nostril) (obtained by a clinician).

Transport media: none reported

Sample storage: none required

Test operator: at primary care centres - qualified nurse; at ED - clinician

Definition of test positivity: visual; used according to the manufacturer IFU

Blinding reported: yes (performed before reference standard)

Timing of samples: median 3 (Q1 2–Q3 5) days after symptom onset

Target condition and reference standard(s) Reference standard: RT-PCR performed using manufacturer IFU on Cobas z 480 Analyser (Roche, Basilea, Suiza). Nucleic acid extraction was performed using 300 µL NP specimen on Chemagic 360 Nucleic Acid Purification Instrument (PerkinElmer España SL, Madrid, Spain)

Definition of non-COVID cases: single -ve PCR

Genetic target(s): E-gene

Samples used: NP

Timing of reference standard: median 3 (Q1 2–Q3 5) days pso

Blinded to index test: unclear

Incorporated index test: no

Flow and timing Time interval between index and reference tests: simultaneous; paired sample

All participants received same reference standard: yes

Missing data: yes; of 913 only 904 had NP (< 1%), 659 had nasal and 611 had saliva

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes Funding: "this work was supported by the RD16/0025/0038 project as a part of the Plan Nacional Research + Development + Innovation (R+D+I) and co-financed by Instituto de Salud Carlos III - Subdirección General de Evaluación y Fondo Europeo de Desarrollo Regional; Instituto de Salud Carlos III (Fondo de Investigaciones Sanitarias (Grant Numbers PI16/01740, PI18/01861; CM 19/00160, COV20-00005)."

Publication status: published

Masia 2021 [A] (Continued)

Source: Open Forum Infectious Diseases

Author COI: authors reported 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		

Masia 2021 [A] (Continued)

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Low risk

Masia 2021 [B]
Study characteristics

Patient Sampling Comparative study of an Ag test on 3 different sample types; [Masia 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of an Ag test on 3 different sample types; [Masia 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests

Test name: Panbio COVID-19 Ag RTD

Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany

Antibody: nucleocapsid

Ag target: not reported

Test method: CGIA

Samples used at primary care centres:

[A] NP swabs (1 swab for each nostril) (qualified nurse)

[B] nasal swab (from 1 nostril) (qualified nurse)

[C] saliva (patients repeatedly spit up to a minimum of 1 mL of saliva into a 100-mL sterile empty container) (self-collected)

Samples used at the ED:

[A] NP swab (1 swab for each nostril) (obtained by a clinician)

Transport media: none reported

Sample storage: none required

Masia 2021 [B] (Continued)

Test operator: at primary care centres - qualified nurse; at ED - clinician

Definition of test positivity: visual; used according to the manufacturer IFU

Blinding reported: yes (performed before reference standard)

Timing of samples: median 3 (Q1 2–Q3 5) days after symptom onset

Target condition and reference standard(s)	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.

Masia 2021 [C]

Study characteristics

Patient Sampling	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: Panbio COVID-19 Ag RTD</p> <p>Manufacturer: Abbott Rapid Diagnostic Jena GmbH, Jena, Germany</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not reported</p> <p>Test method: CGIA</p> <p>Samples used at primary care centres: [A] NP swabs (1 swab for each nostril) (qualified nurse) [B] nasal swab (from 1 nostril) (qualified nurse) [C] saliva (patients repeatedly spit up to a minimum of 1 mL of saliva into a 100-mL sterile empty container) (self-collected)</p> <p>Samples used at the ED: [A] NP swab (1 swab for each nostril) (obtained by a clinician)</p> <p>Transport media: none reported</p> <p>Sample storage: none required</p> <p>Test operator: at primary care centres- qualified nurse; at ED - clinician</p> <p>Definition of test positivity: visual; used according to the manufacturer IFU</p> <p>Blinding reported: yes (performed before reference standard)</p> <p>Timing of samples: median 3 (Q1 2– Q3 5) days after symptom onset</p>

Masia 2021 [C] *(Continued)*

Target condition and reference standard(s)	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of an Ag test on 3 different sample types; Masia 2021 [A] reports full study characteristics and QUADAS.

Merino 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: multicentre study of individuals who had at least 1 symptom compatible with COVID-19 (n = 830) or had been in close contact with a diagnosed COVID-19 patient (n = 128) (total n = 958); all tested within 7 days of symptom onset or exposure</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 958 (359)</p>
Patient characteristics and setting	<p>Setting: hospital EDs or other hospital units (documented only in preprint version)</p> <p>Location: Madrid: Hospital Clínico Universitario San Carlos, Hospital Universitario Ramón y Cajal, Hospital Universitario La Paz, Hospital Universitario Doce de Octubre, and Hospital Universitario Gregorio Marañón. Basque: Hospital Universitario Araba, Hospital Universitario Cruces, Hospital Universitario Basurto, Hospital Universitario Donostia, and Hospital Universitario Galdakao Usansolo</p> <p>Country: Spain</p> <p>Dates: September-October 2020</p> <p>Symptoms and severity: symptomatic 830, 87%; all had at least 1 symptom compatible with COVID-19</p> <p>Demographics: mean age of 42.4 years (range, 1-100 years); 61.3% were women</p> <p>Exposure history: 128 asymptomatic participants had had close contact with COVID-19 patient</p>
Index tests	<p>Test name: PanBio RT COVID-19 Ag Rapid Test Device</p> <p>Manufacturer: Abbott Diagnostics</p> <p>Antibody: nucleocapsid protein</p> <p>Ag target: not reported</p> <p>Test method: CGIA</p> <p>Samples used: NP</p> <p>Transport media: none</p>

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Merino 2021 (Continued)

	<p>Sample storage: immediate</p> <p>Test operator: trained personnel; physicians and nurses from emergency services trained by microbiology specialists</p> <p>Definition of test positivity: according to manufacturer IFU</p> <p>Blinding reported: yes; conducted first</p> <p>Timing of samples: < 7 days pso or COVID exposure; unclear if collected by HCW or self-collected</p>
Target condition and reference standard(s)	<p>Reference standard: PCR; multiple assays used across 10 sites</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): not mentioned</p> <p>Samples used: NP; paired</p> <p>Timing of reference standard: same as for index</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: taken at the same time</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: no external funding was received for this work</p> <p>Publication status: published</p> <p>Source: Clinical Microbiology and Infection</p> <p>Author COI: "RC has participated in educational programmes organized by Abbott. The other authors declare that they have no conflicts of interest."</p>

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		

Merino 2021 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

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Merino 2021 (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Mertens 2020
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity for diagnosis of active disease: samples from symptomatic patients suspected of SARS-COV-2 infections (n = 328)

Recruitment: random sampling of samples submitted to 3 laboratories
 322/328 NP samples (NP swabs) were randomly selected

Prospective or retrospective: retrospective

Number of samples (samples with confirmed SARS-CoV-2): 328 (132)

Patient characteristics and setting Setting: unclear; samples from university laboratories (Discussion states that no outpatient population has been sampled, therefore assume inpatients and HCW samples)

Location: laboratories at Université Libre de Bruxelles (LHUB-ULB), UZ Leuven and Centre Hospitalier Universitaire Sart-Tilman (CHU) Liège

Country: Belgium

Dates: 19-30 March 2020

Symptoms and severity: all described as symptomatic

Demographics: not reported

Exposure history: unclear; 53/328 samples were from HCW

Index tests Test name: COVID-19 Ag Respi-Strip

Manufacturer: Coris BioConcept (Belgium)

Ag target: SARS-CoV and SARS-CoV-2 highly conserved nucleoprotein

Antibody: monoclonal antibodies directed against SARS-CoV and SARS-CoV-2 highly conserved nucleoprotein antigen

Test method: immunochromatographic assay using colloidal gold (CGIA)

Samples used: remnant respiratory specimens (322 NP swabs, 4 NP aspirate and 2 BAL)

Transport media: NP: flocked swab + UTM 3 mL (or 1 mL of Amies) (Copan, Brescia, Italy);
 NPA: 3 mL VTM (veal infusion broth (Difco, Becton Dickinson, Sparks, MD, USA) supplemented with bovine albumin (Sigma Aldrich, St Louis, MO, USA))
 BAL: N/A

Sample storage: not described

Test operator: laboratory technician

Definition of test positivity: visible reddish-purple band appearing at the test line position (T)

Blinding reported: not stated

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Mertens 2020 (Continued)

	Timing of samples: not clear
Target condition and reference standard(s)	<p>Reference standard: qRT-PCR: RealStar SARS-CoV-2 RT-PCR Kit from Altona-diagnostics with a cut-off set at 40 Ct (LHUB-ULB); Roche LC480 thermocycler using Taqman Fast Virus 1-Step Master Mix (Thermo Fisher) (Liege); QuantStudio Dx (Thermo Fisher Scientific) or Panther Fusion (PF, Hologic, San Diego, USA) (UZ Leuven)</p> <p>Definition of non-COVID cases:</p> <ul style="list-style-type: none"> Genetic target(s): RealStar: not stated Taqman Fast Virus: RdRp and E genes QuantStudio Dx; "slightly adapted" E-gene Panther Fusion: E gene and ORF1-ab <p>Samples used: as for index test (NP samples)</p> <p>Timing of reference standard: not stated; same samples as for index test but analysed at time of collection</p> <p>Blinded to index test: yes (undertaken for diagnostic purposes at time of collection)</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same samples used; Discussion reports "some delay" between PCR and Ag testing</p> <p>All participants received same reference standard: yes but different RT-PCR kits</p> <p>Missing data: none reported, no participant flow diagram reported</p> <p>Uninterpretable results: none reported; discussion reports some difficulties in visualising the strip through the closed tube requiring the lab technician to open the test tube in the laminar air flow cabinet and pull out the strip with forceps</p> <p>Indeterminate results (index test): weak T lines considered positive</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: refers to participants</p>
Comparative	
Notes	<p>Funding: not stated</p> <p>Publication status: preprint (not peer-reviewed)</p> <p>Source: medRxiv</p> <p>Author COI: "the IVD medical device has been developed by the investigator Pascal Mertens, Henri Magein, and Justine Bouzet working for Coris BioConcept (potential conflict of interest declared even though they don't have any share in this company); Thierry Leclipteux was involved in the development of this test and is the CEO of Coris Bioconcept (potential conflict of interest declared). All scientific investigators that are external to Coris BioConcept declare having no conflict of interest."</p>

Methodological quality

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

Mertens 2020 (Continued)

Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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?		High
DOMAIN 2: Index Test (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	
If a threshold was used, was it pre-specified?	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?		High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by		High

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Mertens 2020 *(Continued)*
the reference standard does not match the question?
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Miyakawa 2021 [A]
Study characteristics

Patient Sampling 2-group study estimating sensitivity and specificity:
 [1] remnant RT-PCR+ve NP swab specimens (n = 45)
 [2] RT-PCR-ve NP swabs (n = 63; only 45/63 samples tested with 4 of the 5 evaluated assays)

Recruitment: not reported

Prospective or retrospective: retrospectively

Sample size (cases): 108 (45)

Patient characteristics and setting Setting: not reported (laboratory-based at a biosafety level 3 laboratory)

Location: Yokohama City University School of Medicine

Country: Japan

Dates: not reported

Symptoms and severity: not reported

Demographics: not reported

Exposure history: not reported

Index tests

Test name:

[A] authors' own-developed Ag-RDT (YCU-FF LFIA (Ag-RDT); now marketed as **FUJIFILM COVID-19 Ag Test** www.fujifilm.com/jp/en/news/hq/358e)

[B] Panbio COVID-19 Ag Rapid Test

[C] Espline SARS-CoV-2

[D] STANDARD Q COVID-19 Ag

Miyakawa 2021 [A] (Continued)

Also evaluated [E] SARS-CoV-2 Rapid Antigen Test from Roche. Data not included as this is understood to be the same test as 'STANDARD Q' from SD Biosensor

Manufacturer:

[A] **FUJIFILM**

[B] Abbott

[C] Fujirebio

[D] SD Biosensor

Antibody: [A] SARS-CoV-2 nucleocapsid protein; [B] to [D] not described

Ag target: [A] specific monoclonal antibodies against the SARS-CoV-2 nucleocapsid protein; [B] to [D] not described

Test method: [A] CGIA with silver ions; [B] to [D] not described

Samples used: NP (collection not described)

Transport media: VTM (no further detail reported)

Sample storage: stored at -80 °C until used (timing not reported)

Test operator: not reported; "test line interpretations ... made by at least two people"

Definition of test positivity: appearance of visible line

Blinding reported: not stated

Timing of samples: not reported

Target condition and reference standard(s)

Reference standard: RT-qPCR with N2 primer/probe set targeting the N gene

Definition of non-COVID cases: as for cases; presume single negative

Genetic target(s): N gene

Samples used: NP

Timing of reference standard: not reported

Blinded to index test: yes; conducted first

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous (same swab)

All participants received same reference standard: yes

Missing data: not reported

Uninterpretable results: not reported

Indeterminate results (index test): not reported

Indeterminate results (reference standard): not reported

Unit of analysis: participant

Comparative

Notes

Funding: "this work was supported in part by Japan Agency for Medical Research and Development, and by Health Labour Sciences research grant from The Ministry of Health Labour and Welfare to AR"

Miyakawa 2021 [A] (Continued)

Publication status: preprint (not peer reviewed)

Source: medRxiv

Author COI: "YY is an employee of Kanto Chemical Co., Inc.; JK, AW, and TT are current employee of FUJIFILM Corporation"; Remaining authors declare that they have 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		

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Miyakawa 2021 [A] *(Continued)*

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Miyakawa 2021 [B]
Study characteristics

Patient Sampling Comparative study of 4 Ag tests; [Miyakawa 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 4 Ag tests; [Miyakawa 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Test name:

[A] authors' own-developed Ag-RDT (YCU-FF LFIA (Ag-RDT); now marketed as FUJIFILM COVID-19 Ag Test www.fujifilm.com/jp/en/news/hq/358e)
[B] Panbio COVID-19 Ag Rapid Test
 [C] Espline SARS-CoV-2
 [D] STANDARD Q COVID-19 Ag

Also evaluated [E] SARS-CoV-2 Rapid Antigen Test from Roche. Data not included as this is understood to be the same test as 'STANDARD Q' from SD Biosensor

Manufacturer:

[A] FUJIFILM
[B] Abbott
 [C] Fujirebio

[D] SD Biosensor

Antibody: [A] SARS-CoV-2 nucleocapsid protein; [B] to [D] not described

Ag target: [A] specific monoclonal antibodies against the SARS-CoV-2 nucleocapsid protein; [B] to [D] not described

Test method: [A] CGIA with silver ions; [B] to [D] not described

Miyakawa 2021 [B] *(Continued)*

Samples used: NP (collection not described)

Transport media: VTM (no further detail reported)

Sample storage: stored at -80 °C until used (timing not reported)

Test operator: not reported; "test line interpretations ... made by at least two people"

Definition of test positivity: appearance of visible line

Blinding reported: not stated

Timing of samples: not reported

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Miyakawa 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Miyakawa 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Miyakawa 2021 [A] reports full study characteristics and QUADAS.

Miyakawa 2021 [C]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Miyakawa 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	
Index tests	<p>Test name:</p> <p>[A] authors' own-developed Ag-RDT (YCU-FF LFIA (Ag-RDT); now marketed as FUJIFILM COVID-19 Ag Test www.fujifilm.com/jp/en/news/hq/358e)</p> <p>[B] Panbio COVID-19 Ag Rapid Test</p> <p>[C] Espline SARS-CoV-2</p> <p>[D] STANDARD Q COVID-19 Ag</p> <p>Also evaluated [E] SARS-CoV-2 Rapid Antigen Test from Roche. Data not included as this is understood to be the same test as 'STANDARD Q' from SD Biosensor</p> <p>Manufacturer:</p> <p>[A] FUJIFILM</p> <p>[B] Abbott</p> <p>[C] Fujirebio</p> <p>[D] SD Biosensor</p> <p>Antibody: [A] SARS-CoV-2 nucleocapsid protein; [B] to [D] not described</p> <p>Ag target: [A] Specific monoclonal antibodies against the SARS-CoV-2 nucleocapsid protein; [B] to [D] not described</p> <p>Test method: [A] CGIA with silver ions; [B] to [D] not described</p> <p>Samples used: NP (collection not described)</p>

Miyakawa 2021 [C] (Continued)

Transport media: VTM (no further detail reported)

Sample storage: stored at -80 °C until used (timing not reported)

Test operator: not reported; "test line interpretations ... made by at least two people"

Definition of test positivity: appearance of visible line

Blinding reported: not stated

Timing of samples: not reported

Target condition
and reference stan-
dard(s)

Flow and timing Comparative study of 4 Ag tests; [Miyakawa 2021 \[A\]](#) reports full study characteristics and QUADAS.

Comparative

Notes Comparative study of 4 Ag tests; [Miyakawa 2021 \[A\]](#) reports full study characteristics and QUADAS.

Miyakawa 2021 [D]

Study characteristics

Patient Sampling Comparative study of 4 Ag tests; [Miyakawa 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteris-
tics and setting Comparative study of 4 Ag tests; [Miyakawa 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Test name:

[A] authors' own-developed Ag-RDT (YCU-FF LFIA (Ag-RDT); now marketed as FUJIFILM COVID-19 Ag Test www.fujifilm.com/jp/en/news/hq/358e)

[B] Panbio COVID-19 Ag Rapid Test

[C] Espline SARS-CoV-2

[D] STANDARD Q COVID-19 Ag

Also evaluated [E] SARS-CoV-2 Rapid Antigen Test from Roche. Data not included as this is understood to be the same test as 'STANDARD Q' from SD Biosensor

Manufacturer:

[A] FUJIFILM

[B] Abbott

[C] Fujirebio

[D] SD Biosensor

Antibody: [A] SARS-CoV-2 nucleocapsid protein; [B] to [D] not described

Ag target: [A] specific monoclonal antibodies against the SARS-CoV-2 nucleocapsid protein; [B] to [D] not described

Test method: [A] CGIA with silver ions; [B] to [D] not described

Samples used: NP (collection not described)

Transport media: VTM (no further detail reported)

Miyakawa 2021 [D] *(Continued)*

Sample storage: stored at -80 °C until used (timing not reported)

Test operator: not reported; "test line interpretations ... made by at least two people"

Definition of test positivity: appearance of visible line

Blinding reported: not stated

Timing of samples: not reported

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Miyakawa 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Miyakawa 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Miyakawa 2021 [A] reports full study characteristics and QUADAS.

Mockel 2021(a)
Study characteristics

Patient Sampling	<p>Single-group sensitivity and specificity study: patients attending hospital EDs: [1] 4 adult EDs (n = 281); [2] 1 paediatric ED (n = 202) We included cohort [2] as Mockel 2021(b). In both cohorts patients were either symptomatic (acute respiratory symptoms or loss of smell or taste), contacts of confirmed cases up to 14 d before onset of COVID-19 symptoms, or had clinical or radiological signs of viral pneumonia in the context of an outbreak in nursing homes or hospitals.</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 281 (89)</p>
Patient characteristics and setting	<p>Setting: hospital EDs: [1] adult, [2] paediatric</p> <p>Location: Charité - Universitätsmedizin Berlin, Department of Emergency and Acute Medicine</p> <p>Country: Germany</p> <p>Dates: 12 October-24 November 2020</p> <p>Symptoms and severity: cohort [1] only; respiratory symptoms: 157 (57.9%); loss of smell or taste: 18 (6.6%); contact to confirmed COVID-19 case: 33 (12.2%); radiological signs of viral pneumonia: 11 (0.4%); other symptoms: 140 (51.7%); none: 56 (20.7%)</p> <p>Demographics: age mean 59.7 years; SD 18; range 21-98 years Male 160 (59%)</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: SARS-CoV-2 Rapid Antigen Test</p> <p>Manufacturer: Roche /SD Biosensor</p>

Mockel 2021(a) (Continued)

Antibody: not mentioned
 Ag target: not mentioned
 Test method: not mentioned
 Samples used: NOP (taken by ED nurse)
 Transport media: not mentioned
 Sample storage: immediate
 Test operator: ED nurse (a core ED team alongside written instructions trained the ED nurses)
 Definition of test positivity: consensus of ED nurse and 1 other medical professional
 Blinding reported: yes (assumed done first)
 Timing of samples: not mentioned; time pso only reported for those with FN results: both cohorts' range was 1 to > 7 days

Target condition and reference standard(s)

Reference standard: PCR; Roche Cobas SARS-CoV-2 assay (Penzberg, Germany) or SARS-CoV-2 E-gene assay from TibMolbiol (Berlin, Germany)
 Definition of non-COVID cases: single negative PCR
 Genetic target(s): TibMolbiol was E gene
 Samples used: NOP (paired)
 Timing of reference standard: as for index
 Blinded to index test: yes
 Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous (paired)
 All participants received same reference standard: yes
 Missing data: 10 patients excluded from cohort [1] based on reasons below
 Uninterpretable results: no index test result (n = 6), no PCR result (n = 2)
 Indeterminate results (index test): 1 inconclusive (excluded)
 Indeterminate results (reference standard): 1 inconclusive (excluded)
 Unit of analysis: participant

Comparative

Notes

Funding: "work is based on research funded in part by the German Federal Ministry of Education and Research through projects VARIPath (01KI2021) to VMC and NaFoUniMed-Covid19 (BFAST, FKZ: 01KX2021) to the Charité"
 Publication status: accepted manuscript
 Source: Biomarkers
 Author COI: the authors report no conflicts of interest

Methodological quality

Mockel 2021(a) (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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High

Mockel 2021(a) *(Continued)*
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

Mockel 2021(b)
Study characteristics

Patient Sampling	<p>Single-group sensitivity and specificity study: participants were symptomatic patients attending hospital EDs, [1] 4 adult EDs (n = 271) and [2] 1 paediatric ED (n = 202). We included cohort [1] as Mockel 2021(a).</p> <p>In both cohorts patients were either symptomatic (acute respiratory symptoms or loss of smell or taste), contacts of confirmed cases up to 14 d before onset of COVID-19 symptoms, or had clinical or radiological signs of viral pneumonia in the context of an outbreak in nursing homes or hospitals.</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 202 (25)</p>
Patient characteristics and setting	<p>Setting: hospital EDs: [1] adult, [2] paediatric</p> <p>Location: Charité - Universitätsmedizin Berlin, Department of Emergency and Acute Medicine</p> <p>Country: Germany</p> <p>Dates: 12 October-24 November 2020</p> <p>Symptoms and severity: respiratory symptoms: [2] 120 (59.4%); loss of smell or taste: [2] 1 (0.5%); contact to confirmed COVID-19 case: [2] 37 (18.3%); radiological signs of viral pneumonia: [2] 10 (0.5%); other symptoms: [2] 104 (51.5%); none: [2] 26 (12.9%)</p> <p>Demographics: age mean = 3; [range 1-9] Male 111 (55%)</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: SARS-CoV-2 Rapid Antigen Test</p> <p>Manufacturer: Roche/SD Biosensor</p> <p>Antibody: not mentioned</p>

Mockel 2021(b) (Continued)

	<p>Ag target: not mentioned</p> <p>Test method: not mentioned</p> <p>Samples used: NOP (taken by ED nurse)</p> <p>Transport media: not mentioned</p> <p>Sample storage: immediate</p> <p>Test operator: ED nurse (a core ED team alongside written instructions trained the ED nurses)</p> <p>Definition of test positivity: consensus of ED nurse and 1 other medical professional</p> <p>Blinding reported: yes (assumed done first)</p> <p>Timing of samples: not mentioned; time pso only reported for those with FN results: both cohorts' range was 1 to > 7 days</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Roche Cobas SARS-CoV-2 assay (Penzberg, Germany) or SARS-CoV-2 E-gene assay from TibMolbiol (Berlin, Germany)</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): TibMolbiol was E gene</p> <p>Samples used: OP (paired)</p> <p>Timing of reference standard: as for index</p> <p>Blinded to index test: yes</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous (paired)</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none (exclusions all from cohort [1])</p> <p>Uninterpretable results: none</p> <p>Indeterminate results (index test): none</p> <p>Indeterminate results (reference standard): none</p>
Comparative	
Notes	<p>Funding: work is based on research funded in part by the German Federal Ministry of Education and Research through projects VARIPath (01KI2021) to VMC and NaFoUniMedCovid19 (BFAST, FKZ: 01KX2021) to the Charité</p> <p>Publication status: accepted manuscript</p> <p>Source: Biomarkers</p> <p>Author COI: the authors report no conflicts of interest</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Mockel 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 inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Mockel 2021(b) *(Continued)*

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Nagura-Ikeda 2020
Study characteristics

Patient Sampling	<p>Single-group study of patients with laboratory confirmed COVID-19 referred for isolation and treatment (n = 103); participants had undergone qRT-PCR tests using NP or OP swabs collected at public health institutes or hospitals (presumably symptomatic), asymptomatic patients were tested as a result of mass screening due to an outbreak or family cluster.</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: not reported; samples appear to be collected prospectively but states that patient information was retrospectively collected from the hospital electronic medical records.</p>
Patient characteristics and setting	<p>Setting: inpatient and asymptomatic (admitted or quarantined)</p> <p>Location: Self-Defense Forces Central Hospital, Tokyo</p> <p>Country: Japan</p> <p>Dates: 11 February-13 May 2020</p> <p>Symptoms and severity: 88 (85%) symptomatic, including 16 (15%) severe (showing clinical symptoms of pneumonia - dyspnoea, tachypnoea, saturation of percutaneous oxygen (SpO₂) < 93%, and the need for oxygen therapy); 15 (15%) asymptomatic (including 4 pre-symptomatic)</p> <p>Demographics: IPD provided - median age 46, range 18-87; 66 (64%) male</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: ESPLINE SARS-CoV-2 (no product code reported) (5 other tests performed including RT-PCR and RT-LAMP, but not eligible for this review)</p> <p>Manufacturer: Fuji Rebio Inc</p> <p>Antibody: NP</p> <p>Ag target: not stated</p> <p>Test method: LFA (no reader device required)</p> <p>Samples used: saliva (self-collected)</p> <p>Transport media: none; around 500 µL saliva collected</p> <p>Sample storage: stored at -80 °C until sample preparation</p>

Nagura-Ikeda 2020 (Continued)

	Test operator: not stated; implies laboratory staff Definition of test positivity: not stated; appearance of test line implied Blinding reported: not stated Timing of samples: saliva collected on admission to hospital; IPD reports this was median 7 days pso (1-14)
Target condition and reference standard(s)	Reference standard: RT-qPCR on initial presentation (RT-PCR was conducted on saliva samples as part of the study but this did not form part of the reference standard diagnosis) Definition of non-COVID cases: single RT-PCR negative Genetic target(s): not reported Samples used: NP or OP Timing of reference standard: on presentation or as part of mass screening; specific timing in regard to symptom onset was not reported for the original RT-PCR and unclear if same day as saliva collection Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: unclear; saliva collected on day of admission to quarantine/hospital but NP/OP conducted at some point prior to that All participants received same reference standard: yes Missing data: not stated, no participant flow diagram reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "work was supported by the Health, Labour and Welfare Policy Research Grants, Research on Emerging and Re-emerging Infectious Diseases and Immunization [grant number 20HA2002]". Publication status: accepted manuscript Source: Journal of Clinical Microbiology Author COI: the authors declare that they have no conflicts of 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?	No		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Nagura-Ikeda 2020 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Nagura-Ikeda 2020 (Continued)

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Nalumansi 2020
Study characteristics

Patient Sampling	<p>2-group study to estimate sensitivity and specificity:</p> <ol style="list-style-type: none"> COVID-19 cases (PCR+) identified from regional referral hospitals (n = 90); discussion describes 89% as asymptomatic PCR-ve controls were volunteers at a Military Barracks and the Uganda Virus Research Institute clinic. (n = 172) <p>Recruitment: not reported</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 262 (90)</p>
Patient characteristics and setting	<p>Setting: unclear; referral hospitals (also described as COVID-19 treatment facilities)</p> <p>Location: regional referral hospitals (RRHs) in Arua, Entebbe, Fort Portal, Gulu, Jinja, Lira, Masaka, Mbale, and Mulago National Referral Hospital. (Uganda Virus Research Institute, Entebbe, Uganda)</p> <p>Country: Uganda</p> <p>Dates: not reported</p> <p>Symptoms and severity: mainly asymptomatic: 77/90 (89%) PCR+ (described in Discussion only); 172 PCR-</p> <p>Demographics: mean age 37 (95% CI 35-39) years; male 85 (94%)</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test</p> <p>Manufacturer: SD Biosensor, Gyeonggi-do, 16690, Korea</p> <p>Antibody: Ag</p> <p>Ag target: not reported</p> <p>Test method: CGIA</p> <p>Samples used: nasal (laboratory staff)</p> <p>Transport media: none used</p>

Nalumansi 2020 (Continued)

	<p>Sample storage: not required; immediate on-site testing</p> <p>Test operator: laboratory staff (training not reported)</p> <p>Definition of test positivity: visual; according to the manufacturer IFU</p> <p>Blinding reported: no; described as "unblinded" ("the staff who evaluated the Ag RDT knew which participants were likely to be infected or uninfected in most cases)</p> <p>Timing of samples: not recorded</p>
Target condition and reference standard(s)	<p>Reference standard: qRT-PCR (Berlin protocol); used Applied Biosystems PCR platform and QIAGEN viral RNA mini kit</p> <p>Ct values were categorized as strongly positive (Ct ≤ 29) indicating abundant target nucleic acid in the sample, moderately positive (Ct 30–37), and weakly positive (Ct 38–39).</p> <p>Definition of non-COVID cases: same as for cases</p> <p>Genetic target(s): not reported</p> <p>Samples used: nasal; paired</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: yes; Ag interpretation was not blinded to SARS-CoV-2 status so PCR must have been undertaken first</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous swab; same sample site</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "no specific funding was received"</p> <p>Publication status: published</p> <p>Source: International Journal of Infectious Diseases</p> <p>Author COI: all authors declare no competing interests</p>

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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Nalumansi 2020 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? No

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Nalumansi 2020 (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Nash 2020
Study characteristics

Patient Sampling Unclear design to estimate sensitivity and specificity: samples from suspected patients submitted to 'PATH' (www.path.org) for routine COVID diagnosis (Second cohort of samples also tested using spike-based assay; excluded as assay requires use of centrifuge)

Recruitment: not stated

Prospective or retrospective: retrospective

Patient characteristics and setting Setting: unclear; samples provided to study authors by PATH (non-profit organisation), protocol number 00004244

Location: not reported

Country: not reported

Dates: not reported

Symptoms and severity: not reported

Demographics: not reported

Exposure history: not reported

Index tests Test name: Direct antigen rapid test (DART); NP-based

Manufacturer: E25Bio Inc (Cambridge MA); not yet available

Antibody: NP

Ag target: anti-N mouse monoclonal antibodies

Test method: immunochromatographic paper-based (CGIA)

Samples used: nasal; collection not described

Transport media: not stated

Sample storage: banked frozen prior to testing

Test operator: not stated; presume lab staff

Definition of test positivity: visual line

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s) Reference standard: qRT PCR; ThermoFisher/AppliedBiosystems TaqPATH COVID-19 Combo Kit (ThermoFisher, Waltham, MA USA)

Nash 2020 (Continued)

	Definition of non-COVID cases: as for cases; single negative PCR required Genetic target(s): N, S, and ORF1ab genes Samples used: nasal (same swab) Timing of reference standard: not stated Blinded to index test: yes, conducted first Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous (same swab) All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: not stated
Comparative	
Notes	Funding: "the study is funded, in part, by a Bill and Melinda Gates Foundation Award (INV-017872) to E25Bio, Inc. EN is funded by Tufts University DISC Seed Grant. MLN is supported by a FAPESP grant (#2020/04836-0) and is a CNPq Research Fellow. AFV is supported by a FAPESP Fellow grant (#18/17647-0). GRFC is supported by a FAPESP Fellow grant (#20/07419-0). BHGAM 798 is supported by a FAPESP Scholarship (#19/06572-2)." Publication status: preprint Source: medRxiv Author COI: "BN, AB, AR, MB, NS, AG, IB, and BBH are employed by or affiliated with E25Bio Inc. (www.e25bio.com), a company that develops diagnostics for epidemic viruses."

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 inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	

Nash 2020 (Continued)

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Ngo Nsoga 2021

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: patients attending a single COVID-19 screening centre either with symptoms compatible with COVID-19 infection or asymptomatic contacts (The results of a separate pilot study is reported in a supplementary appendix however details are limited.)</p> <p>Recruitment: unclear</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 402 (168)</p>
Patient characteristics and setting	<p>Setting: outpatient COVID-19 screening site</p> <p>Location: Geneva; Geneva University Hospital</p> <p>Country: Switzerland</p> <p>Dates: 3-12 November 2020</p> <p>Symptoms and severity: states that the "majority" were symptomatic, and that all 168 PCR+ve were symptomatic. Appears that symptom breakdown was only provided for these 168. Symptoms included: asthenia 101 (60.1%); headache 99 (48.9%); myalgia 81 (48.2%); chills/fever 80 (47.6%); dry/productive cough 73 (43.5%); anosmia/ageusia 71 (42.3%); odynophagia 68 (40.5%); digestive signs 38 (22.6%); dyspnoea 7 (4.2%); chest pain 4 (2.4%); other 12 (7.1%)</p> <p>Demographics: age: mean 39.9 years; SD +/-14.5 years; median 38 years; range 16-80 years. Male: 178 (44.3%)</p> <p>Exposure history: contact with positive case in last 14 days: 87/168 (51.8%)</p>
Index tests	<p>Test name: PanBio Ag RDT</p> <p>Manufacturer: Abbot</p> <p>Antibody: not mentioned</p> <p>Ag target: not mentioned</p> <p>Test method: CGIA</p> <p>Samples used: OP; collected by experienced doctor. Pilot study suggested poor sensitivity when back of pharynx was not reached</p> <p>Transport media: not mentioned</p> <p>Sample storage: not mentioned</p> <p>Test operator: states "biologist" with a second HCW for equivocal results</p> <p>Definition of test positivity: according to manufacturer IFU</p> <p>Blinding reported: not mentioned</p> <p>Timing of samples: samples obtained up to 24 d pso. (Figure 1); text reports 101 day 0-4; 19 day 5-7; 17 day 8-11; mean 4.1 days pso to PCR (range 0-24 d)</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Cobas SARS-CoV-2 RT-PCR assay</p> <p>Definition of non-COVID cases:</p>

Ngo Nsoga 2021 (Continued)

Genetic target(s): ORF1 and E gene

Samples used: NP; collected by nurse

Timing of reference standard: as for index test; some asymptomatic cases and no information on these timings

Blinded to index test: not mentioned

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: assumed same time but not clear

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): 2 samples were positive for ORF1 only and not E gene - interpreted as positive

Unit of analysis: participant

Comparative

Notes

Funding: "this work was supported by Foundation of Innovative Diagnostics (FIND), by Private HUG Foundation and by Pictet Charitable Foundation. Marie Thérèse Ngo Nsoga is a beneficiary of the excellence grant from the Swiss Confederation and the grant from the humanitarian commission of the University Hospital of Geneva"

Publication status: preprint

Source: preprint

Author COI: none mentioned

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 inclusions?	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 (Evaluations of single test application)			

Ngo Nsoga 2021 (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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?		High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Nikolai 2021(a) [A]
Study characteristics

Patient Sampling	<p>2 single-group studies to estimate sensitivity and specificity: [1] symptomatic adults with high clinical suspicion of COVID-19 presenting at an ambulatory SARS-CoV-2 testing facility (compared professionally collected AN and NMT samples) (n = 132) [2] symptomatic adults with high clinical suspicion of COVID-19 presenting at an ambulatory SARS-CoV-2 testing facility (compared self-collected NMT sample and professional NP swab) (n = 96); see Nikolai 2021(b) [A] for further details</p> <p>Recruitment: consecutively enrolled (according to laboratory capacity)</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 132 (36)</p>
Patient characteristics and setting	<p>Setting: ambulatory SARS-CoV-2 testing facility</p> <p>Location: Charité University Hospital</p> <p>Country: Germany</p> <p>Dates: 30 November 2020-18 January 2021</p> <p>Symptoms and severity: whole sample (n = 228): 222, 97.4% of participants had ≥ 1 symptoms consistent with SARS-CoV-2 infection</p> <p>Demographics: average age: 34.6 years (SD 11.7) Sex: 107, 47% female</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test (nasal sampling kit used; RUO at time of study)</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea (also distributed by Roche in Europe)</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: 2 types of samples for each patient: [A] AN (both nostrils) [B] NMT (both nostrils) (both collected by professional following CDC guidance for SARS-CoV-2 testing; sequence of sampling alternated between patients)</p> <p>Transport media: none</p> <p>Sample storage: directly after sampling</p> <p>Test operator: study physicians</p> <p>Definition of test positivity: semi-quantitative visual read-out of the test band (2 independent blinded readers)</p> <p>Blinding reported: yes</p> <p>Timing of samples: whole sample (n = 228): mean 3.4 days (SD 3.0)</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR (no further details reported; cites Lindner 2021b [A])</p> <p>Definition of non-COVID cases: as for cases</p>

Nikolai 2021(a) [A] (Continued)

Genetic target(s): not reported

Samples used: OP/NP sampling (collected by professional after AN, NMT swabs)

Timing of reference standard: same as for index test

Blinded to index test: not reported

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous

All participants received same reference standard: yes

Missing data: yes; 2 exclusions from whole sample of 230 enrolled

Uninterpretable results: not reported

Indeterminate results (index test): not reported

Indeterminate results (reference standard): 2 invalid RT-PCR results

Unit of analysis: participant

Comparative

Notes

Funding: "CM Denkinger reports grants from Foundation of Innovative New Diagnostics, grants from Ministry of Science, Research and Culture, State of Baden Wuerttemberg, Germany, to conduct of the study. JA Sacks reports grants from UK Department of International Development (DFID, recently replaced by FCMO), grants from World Health Organization (WHO), grants from Unitaid, to conduct of the study."

Publication status: preprint (not peer reviewed)

Source: medRxiv

Author COI: all authors declare 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			

Nikolai 2021(a) [A] *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Nikolai 2021(a) [B]
Study characteristics

Patient Sampling	Comparative study of 2 sample types collected professionally; Nikolai 2021(a) [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 2 sample types collected professionally; Nikolai 2021(a) [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: STANDARD Q COVID-19 Ag Test (nasal sampling kit used; RUO at time of study)</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea (also distributed by Roche in Europe)</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: 2 types of samples for each patient: [A] AN (both nostrils) [B] NMT (both nostrils) (both collected by professional following CDC guidance for SARS-CoV-2 testing; sequence of sampling alternated between patients)</p> <p>Transport media: none</p> <p>Sample storage: directly after sampling</p> <p>Test operator: study physicians</p> <p>Definition of test positivity: semi-quantitative visual read-out of the test band (2 independent blinded readers)</p> <p>Blinding reported: yes</p> <p>Timing of samples: whole sample (n = 228): mean 3.4 days (SD 3.0)</p>
Target condition and reference standard(s)	Comparative study of 2 sample types collected professionally; Nikolai 2021(a) [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 sample types collected professionally; Nikolai 2021(a) [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 sample types collected professionally; Nikolai 2021(a) [A] reports full study characteristics and QUADAS.

Nikolai 2021(b) [A]
Study characteristics

Patient Sampling	<p>2 single-group studies to estimate sensitivity and specificity: [1] symptomatic adults with high clinical suspicion of COVID-19 presenting at an ambulatory SARS-CoV-2 testing facility (compared professionally collected AN and NMT samples) (n = 132); see Nikolai 2021(a) [A] for further details</p>
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Nikolai 2021(b) [A] (Continued)

[2] symptomatic adults with high clinical suspicion of COVID-19 presenting at an ambulatory SARS-CoV-2 testing facility (compared self-collected NMT sample and professional NP swab) (n = 96)

Recruitment: consecutively enrolled (according to laboratory capacity)

Prospective or retrospective: prospectively

Sample size (cases): 96 (34)

 Patient characteristics and setting

Setting: ambulatory SARS-CoV-2 testing facility

Location: Charité University Hospital

Country: Germany

Dates: 30 November 2020-18 January 2021

Symptoms and severity: whole sample (n = 228): 222, 97.4% of participants had ≥ 1 symptoms consistent with SARS-CoV-2 infection

Demographics: average age: 34.6 years (SD 11.7)

Sex: 107, 47% female

Exposure history: not reported

 Index tests

Test name: **[A] STANDARD Q COVID-19 Ag Test (nasal sampling kit; RUO)**
[B] STANDARD Q COVID-19 Ag Test (NP sampling kit)

Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea (also distributed by Roche in Europe)

Antibody: not reported

Ag target: not reported

Test method: not reported

Samples used: 2 types of samples for each patient:
[A] NMT (self-sampling, both nostrils; observed without intervention) and
[B] NP (1 nostril; collected by professional)

Transport media: none

Sample storage: directly after sampling

Test operator: study physicians

Definition of test positivity: semi-quantitative visual read-out of the test band (2 independent blinded readers)

Blinding reported: yes

Timing of samples: whole sample (n = 228): mean 3.4 days (SD 3.0)

 Target condition and reference standard(s)

Reference standard: RT-PCR (no further details reported; cites [Lindner 2021b \[A\]](#))

Definition of non-COVID cases: as for cases

Genetic target(s): not reported

Samples used: OP/NP sampling (other nostril to NP swab for Ag test; collected by professional after other swabs)

Timing of reference standard: same as for index test

Blinded to index test: not reported

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Nikolai 2021(b) [A] (Continued)

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous

All participants received same reference standard: yes

Missing data: yes; 2 exclusions from whole sample of 230 enrolled

Uninterpretable results: not reported

Indeterminate results (index test): not reported

Indeterminate results (reference standard): 2 invalid RT-PCR results

Unit of analysis: participant

Comparative

Notes

Funding: "CM Denkinger reports grants from Foundation of Innovative New Diagnostics, grants from Ministry of Science, Research and Culture, State of Baden Wuerttemberg, Germany, to conduct of the study. JA Sacks reports grants from UK Department of International Development (DFID, recently replaced by FCMO), grants from World Health Organization (WHO), grants from Unitaid, to conduct of the study."

Publication status: preprint (not peer reviewed)

Source: medRxiv

Author COI: all authors declare 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		

Nikolai 2021(b) [A] *(Continued)*

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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Low risk

Nikolai 2021(b) [B]
Study characteristics

Patient Sampling Comparative study of 2 sample types collected professionally versus self-collected; [Nikolai 2021\(b\) \[A\]](#) reports full study characteristics and QUADAS.

Nikolai 2021(b) [B] (Continued)

Patient characteristics and setting	Comparative study of 2 sample types collected professionally versus self-collected; Nikolai 2021(b) [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] STANDARD Q COVID-19 Ag Test (nasal sampling kit; RUO) [B] STANDARD Q COVID-19 Ag Test (NP sampling kit)</p> <p>Manufacturer: SD Biosensor, Inc. Gyeonggi-do, Korea (also distributed by Roche in Europe)</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: not reported</p> <p>Samples used: 2 types of samples for each patient: [A] NMT (self-sampling, both nostrils; observed without intervention) and [B] NP (1 nostril; collected by professional)</p> <p>Transport media: none</p> <p>Sample storage: directly after sampling</p> <p>Test operator: study physicians</p> <p>Definition of test positivity: semi-quantitative visual read-out of the test band (2 independent blinded readers)</p> <p>Blinding reported: yes</p> <p>Timing of samples: whole sample (n = 228): mean 3.4 days (SD 3.0)</p>
Target condition and reference standard(s)	Comparative study of 2 sample types collected professionally versus self-collected; Nikolai 2021(b) [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 sample types collected professionally versus self-collected; Nikolai 2021(b) [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 sample types collected professionally versus self-collected; Nikolai 2021(b) [A] reports full study characteristics and QUADAS.

Okoye 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: asymptomatic college age (undergraduate and graduate) students; not experiencing signs or symptoms of COVID-19 at the time of testing</p> <p>Recruitment: not stated; likely consecutive</p> <p>Prospective or retrospective: prospectively</p> <p>Sample size (cases): 2645 (46)</p>
Patient characteristics and setting	<p>Setting: temporary indoor testing site</p> <p>Location: University of Utah in Salt Lake City, Utah</p>

Okoye 2021 (Continued)

Country: USA

Dates: 13 November-20 November 2020

Symptoms and severity: asymptomatic

Demographics: average age: 24 years (range: 15-86 years)

Sex: 52% female

Exposure history: not reported

Index tests

Test name: BinaxNOW COVID-19 antigen card

Manufacturer: Abbott

Antibody: SARS-CoV-2 nucleocapsid antigen

Ag target: not reported

Test method: not reported

Samples used: NMT (self-collected, both nostrils according to CDC guidelines, observed by trained non-medical personnel)

Transport media: none (direct swab)

Sample storage: immediate testing

Test operator: trained non-medical personnel (University of Utah Hope Corps interns) according to the manufacturer IFU

Definition of test positivity: 2 pink/purple lines observed

Blinding reported: yes

Timing of samples: not applicable (asymptomatic)

Target condition and reference standard(s)

Reference standard: Thermo Fisher TaqPath COVID-19 Combo kit; 40 cycles performed, ≥ 2 target genes required. Ct was reported as average of the Ct values of the detected coronavirus genes.
PCR+ participants invited to reattend for saliva sampling for second confirmatory RT-PCR (Hologic Panther Fusion SARS-CoV-2 assay, the Roche Cobas SARS-CoV-2 assay, or the Thermo Fisher TaqPath COVID-19 Combo kit)

Definition of non-COVID cases: as for cases

Genetic target(s): ORF1ab, S, N

Samples used: as for index test (NMT), but placed in ARUP COVID-19 Transport Media; order of testing randomly assigned to either Ag or PCR

Timing of reference standard: not applicable (asymptomatic)

Blinded to index test: not reported

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired

All participants received same reference standard: yes

Missing data: yes; 7 excluded

Uninterpretable results: 3 invalid BinaxNOW results; all negative on retesting with new nasal swab specimen

Okoye 2021 (Continued)

Indeterminate results (index test): none

Indeterminate results (reference standard): 4 inconclusive on PCR; only N gene detected (Ct > 30)

Unit of analysis: participant

Comparative

Notes

 Funding: no funding reported
 "The BinaxNOW antigen cards utilized in this study were received from the Utah Department of Health as part of a U.S. federal government initiative"

Publication status: academic journal

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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			

Okoye 2021 (Continued)

Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Low risk

Olearo 2021 [A]
Study characteristics

Patient Sampling	2-groups study to estimate sensitivity and specificity: 1] RT-PCR+ve (n = 84), included until target number met 2] RT-PCR-ve (n = 100), randomly selected to serve as negative control Swabs collected following routine diagnostics from patients hospitalized with suspected or known COVID-19 Recruitment: unclear for RT-PCR+ve; RT-PCR-ve were randomly sampled Prospective or retrospective: retrospective (described as prospective, but samples included based on PCR status) Sample size (cases): 184 (84)
Patient characteristics and setting	Setting: hospital inpatient Location: University Medical Centre Hamburg-Eppendorf, Germany Country: Germany

Olearo 2021 [A] (Continued)

Dates: August–November 2020

Symptoms and severity: median duration pso 6 (IQR 2–12) days

Demographics: not reported

Exposure history: not reported

Index tests

Test name: **[A] SARS-CoV-2 Rapid Antigen Test (Roche)**

[B] COVID-19 Rapid Test Device (Abbott)

[C] MEDsan SARSCoV-2 Antigen Rapid Test

[D] CLINITEST Rapid COVID.19 Antigen Test

Manufacturer: **[A] SD Biosensor (Roche Diagnostics), South Korea**

[B] Panbio Ltd. (Abbott Rapid Diagnostics), Australia

[C] MEDsan GmbH, Germany

[D] Zhejiang Orient Biotech Co, China

Antibody: nucleocapsid

Ag target: not reported

Test method: CGIA

Samples used: OP or NP (HCW)

Transport media: UTM-based collection kits by Copan (Italy, Brescia) or Iclean (Shenzhen, China)

Sample storage: not reported

Test operator: lab technicians; swabs supplied with the Ag kits were immersed in patient OP/NP samples for approximately 10 s before all further steps of the tests were carried out according to manufacturer IFU.

Definition of test positivity: visual

Blinding reported: no; states test results "were read by two unblinded operators"

Timing of samples: median 6 (IQR 2–12) days pso

Target condition and reference standard(s)

Reference standard: RT-qPCR assay (Roche Cobas SARS-CoV-2 IVD) in conjunction with quantitative external control material by Instand e.V. (Düsseldorf, Germany)

Definition of non-COVID cases: same as for cases

Genetic target(s): not reported

Samples used: OP or NP (same sample)

Timing of reference standard: median 6 (IQR 2–12) days from symptom onset

Blinded to index test: yes (performed before index test)

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab used

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Olearo 2021 [A] (Continued)

Indeterminate results (reference standard): none reported

Unit of analysis: participant

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

Source: Journal of Clinical Virology

Author COI: the authors declare no known competing finance

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		

Olearo 2021 [A] (Continued)

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Olearo 2021 [B]
Study characteristics

Patient Sampling Comparative study of 4 Ag tests; [Olearo 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 4 Ag tests; [Olearo 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Test name: [A] SARS-CoV-2 Rapid Antigen Test (Roche)
[B] COVID-19 Rapid Test Device (Abbott)
 [C] MEDsan SARSCoV-2 Antigen Rapid Test
 [D] CLINITEST Rapid COVID.19 Antigen Test

Manufacturer: [A] SD Biosensor (Roche Diagnostics), South Korea
[B] Panbio Ltd. (Abbott Rapid Diagnostics), Australia
 [C] MEDsan GmbH, Germany
 [D] Zhejiang Orient Biotech Co, China

Antibody: nucleocapsid

Ag target: not reported

Test method: CGIA

Samples used: OP or NP (HCW)

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Olearo 2021 [B] (Continued)

Transport media: UTM-based collection kits by Copan (Italy, Brescia) or Iclean (Shenzhen, China)

Sample storage: not reported

Test operator: lab technicians; swabs supplied with the Ag kits were immersed in patient OP/NP samples for approximately 10 s before all further steps of the tests were carried out according to manufacturer IFU.

Definition of test positivity: visual

Blinding reported: no; states test results "were read by two unblinded operators"

Timing of samples: median 6 (IQR 2–12) days pso

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Olearo 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Olearo 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Olearo 2021 [A] reports full study characteristics and QUADAS.

Olearo 2021 [C]

Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Olearo 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Olearo 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] SARS-CoV-2 Rapid Antigen Test (Roche) [B] COVID-19 Rapid Test Device (Abbott) [C] MEDsan SARSCoV-2 Antigen Rapid Test [D] CLINITEST Rapid COVID.19 Antigen Test</p> <p>Manufacturer: [A] SD Biosensor (Roche Diagnostics), South Korea [B] Panbio Ltd. (Abbott Rapid Diagnostics), Australia [C] MEDsan GmbH, Germany [D] Zhejiang Orient Biotech Co, China</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not reported</p> <p>Test method: CGIA</p> <p>Samples used: OP or NP (HCW)</p> <p>Transport media: UTM-based collection kits by Copan (Italy, Brescia) or Iclean (Shenzhen, China)</p> <p>Sample storage: not reported</p> <p>Test operator: lab technicians; swabs supplied with the Ag kits were immersed in patient OP/NP samples for approximately 10 s before all further steps of the tests were carried out according to instructions by manufacturers.</p> <p>Definition of test positivity: visual</p>

Oleario 2021 [C] *(Continued)*

Blinding reported: no; states test results "were read by two unblinded operators"

Timing of samples: median 6 (IQR 2–12) days pso

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Oleario 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Oleario 2021 [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Oleario 2021 [A] reports full study characteristics and QUADAS.

Oleario 2021 [D]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Oleario 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Oleario 2021 [A] reports full study characteristics and QUADAS.
Index tests	<p>Test name: [A] SARS-CoV-2 Rapid Antigen Test (Roche) [B] COVID-19 Rapid Test Device (Abbott) [C] MEDsan SARSCoV-2 Antigen Rapid Test [D] CLINITEST Rapid COVID.19 Antigen Test</p> <p>Manufacturer: [A] SD Biosensor (Roche Diagnostics), South Korea [B] Panbio Ltd. (Abbott Rapid Diagnostics), Australia [C] MEDsan GmbH, Germany [D] Zhejiang Orient Biotech Co, China</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not reported</p> <p>Test method: CGIA</p> <p>Samples used: OP or NP (HCW)</p> <p>Transport media: UTM-based collection kits by Copan (Italy, Brescia) or Iclean (Shenzhen, China)</p> <p>Sample storage: not reported</p> <p>Test operator: lab technicians; swabs supplied with the Ag kits were immersed in patient OP/NP samples for approximately 10 s before all further steps of the tests were carried out according to instructions by manufacturers.</p> <p>Definition of test positivity: visual</p> <p>Blinding reported: no; states test results "were read by two unblinded operators"</p> <p>Timing of samples: median 6 (IQR 2–12) days pso</p>
Target condition and reference standard(s)	Comparative study of 4 Ag tests; Oleario 2021 [A] reports full study characteristics and QUADAS.

Olearo 2021 [D] (Continued)

Flow and timing Comparative study of 4 Ag tests; [Olearo 2021 \[A\]](#) reports full study characteristics and QUADAS.

Comparative

Notes Comparative study of 4 Ag tests; [Olearo 2021 \[A\]](#) reports full study characteristics and QUADAS.

Osterman 2021(a) [A]

Study characteristics

Patient Sampling Multi-site, multiple group study, including:
(1) Site 1: symptomatic patients (adults and children) presenting at EDs or on clinical units (n = 741 swabs, including 381 PCR+ and 360 PCR-); of 381 PCR+, 189 were classed as primary diagnosis (no previous PCR+) and 192 swabs were undertaken at “follow-up” during hospitalization, i.e. at variable time points after onset of symptoms or first PCR+ result

Site 2 extracted as [Osterman 2021\(b\)](#)
(2) Site 2: symptomatic and asymptomatic participants at patient care units or from employee screening, all PCR+ (n = 66)

Recruitment: not mentioned

Prospective or retrospective: unclear; includes frozen samples so not sure we can assume prospective here

Sample size (cases): 833 (447); test [A] FIA 741 (381); test [B] RAT 831 (445)

Patient characteristics and setting Setting: mixed; (1) hospital inpatient and ED

Location: (1) LMU Klinikum Hospital, Munich

Country: Germany

Dates: (1) 4 March-19 October 2020

Symptoms and severity: (1) all symptomatic;
(1) + (2) 256/445 (58%) PCR+ primary diagnosis, and 189/445 (42%) follow-up testing

Demographics: only reported for PCR- at site 1: 326/386 (84%) adults; 60/386 (16%) children

Exposure history: not mentioned

Index tests Test name:

[A] STANDARD F COVID-19 Ag FIA;

[B] SARS-CoV-2 Rapid Antigen Test (RAT)

Manufacturer:

[A] SD Biosensor;

[B] Roche Diagnostics

Ag target: both nucleocapsid

Test method:

[A] FIA;

Osterman 2021(a) [A] (Continued)

[B] CGIA

Samples used: site (1) NP 182; OP 53, sampling site unknown 154; collected by HCWs

Transport media: site (1) eSwab (Copan Diagnostics, Murrieta, California, USA), ImproViral (Improve Medical, Guangzhou, Republic of China) dry swabs inserted into sterile 0.9% NaCl, or the original manufacturers' swabs inserted into the extraction buffers provided

Sample storage: same day

Site (1): were either kept at room temperature for 1–2 h (“fresh”) (n = 18); stored at 4 °C for 0–7 days (n = 48); or stored at –20 °C (n = 315) until SARS-CoV-2 antigen testing was performed

Test operator: laboratory personnel according to manufacturer IFU

Definition of test positivity: [A] a cut-off index (COI) ≥ 1 was interpreted as positive after 30 min [B] every visible (even if very faint or not uniform) test line was interpreted as positive after 15 or 30 min.

Blinding reported: not mentioned

Timing of samples: not mentioned

Target condition and reference standard(s)

Reference standard: PCR; multiple assays used at both sites

Definition of non-COVID cases: not reported

Genetic target(s): site 1: N1 or envelope

Samples used: as for index test; Site 1: OP or NP

Timing of reference standard: not mentioned

Blinded to index test: not mentioned

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: assumed same time

All participants received same reference standard: all received PCR but many types/brands of PCR listed

Missing data: number PCR+ across the 2 sites sums to 447 but maximum number PCR+ reported was 445 (test [B]); only 381 reported for RAT test (site 1)

Uninterpretable results: none mentioned

Indeterminate results (index test): none mentioned

Indeterminate results (reference standard): none mentioned

Unit of analysis: participant

Comparative

Notes

Funding: "Open Access funding enabled and organized by Projekt DEAL. This work was supported in part by the German BMBF initiative “NaFoUniMedCovid19” (01KX2021), subproject B-FAST (to U.P. and O.T.K.), and by the Medical Faculty of the LMU München, Munich, Germany (to O.T. K.)"

Publication status: published

Source: Medical Microbiology and Immunology

Author COI: the authors declare that they have no conflict of interest

Osterman 2021(a) [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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		

Osterman 2021(a) [A] *(Continued)*

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Unclear risk

Osterman 2021(a) [B]
Study characteristics

Patient Sampling Comparative study of 2 Ag tests; [Osterman 2021\(a\) \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting

Index tests

Test name:

[A] STANDARD F COVID-19 Ag FIA;

[B] SARS-CoV-2 Rapid Antigen Test (RAT)

Manufacturer:

[A] SD Biosensor;

[B] Roche Diagnostics

Ag target: both nucleocapsid

Test method:

[A] FIA;

[B] CGIA

Samples used: site (1) NP 182 ; OP 53, sampling site unknown 154; collected by HCWs

Osterman 2021(a) [B] (Continued)

Transport media: site (1) eSwab (Copan Diagnostics, Murrieta, California, USA), ImproViral (Improve Medical, Guangzhou, Republic of China) dry swabs inserted into sterile 0.9% NaCl, or the original manufacturers' swabs inserted into the extraction buffers provided

Sample storage: same day

Site (1): were either kept at room temperature for 1–2 h ("fresh") (n = 18); stored at 4 °C for 0–7 days (n = 48); or stored at –20 °C (n = 315) until SARS-CoV-2 antigen testing was performed

Test operator: laboratory personnel according to manufacturers instructions

Definition of test positivity: [A] a cut-off index (COI) ≥ 1 was interpreted as positive after 30 min

[B] every visible (even if very faint or not uniform) test line was interpreted as positive after 15 or 30 min.

Blinding reported: not mentioned

Timing of samples: not mentioned

Target condition and reference standard(s)	Comparative study of 2 Ag tests; Osterman 2021(a) [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 Ag tests; Osterman 2021(a) [A] reports full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 Ag tests; Osterman 2021(a) [A] reports full study characteristics and QUADAS.

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 inclusions?	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 (Evaluations of single test application)			
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		

Osterman 2021(a) [B] *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?

Did all patients receive the same reference standard?

Were all patients included in the analysis?

Did all participants receive a reference standard?

Could the patient flow have introduced bias?

Osterman 2021(b)
Study characteristics

Patient Sampling	<p>Multi-site, multiple group study, including: (2) Site 2: symptomatic and asymptomatic participants at patient care units or from employee screening, all PCR+ (n = 66)</p> <p>Also reports data for site 1 (included as Osterman 2021(a) [A])</p> <p>(1) Site 1: symptomatic patients (adults and children) presenting at EDs or on clinical units (n = 741 swabs, including 381 PCR+ and 360 PCR-); of 381 PCR+, 189 were classed as primary diagnosis (no previous PCR+) and 192 swabs were undertaken at “follow-up” during hospitalization, i.e. at variable time points after onset of symptoms or first PCR+ result]</p> <p>Recruitment: not mentioned</p> <p>Prospective or retrospective: unclear; includes frozen samples so not sure we can assume prospective here</p> <p>Sample size (cases): 833 (447); test [A] FIA 741 (381); test [B] RAT 831 (445)</p>
Patient characteristics and setting	<p>Setting: mixed; (2) hospital inpatient and employee test centre</p> <p>Location: (2) University Hospital Rechts der Isar of the Technical University of Munich (TUM)</p> <p>Country: Germany</p> <p>Dates: (2) 13 November-8 December 2020</p> <p>Symptoms and severity: (2) symptomatic and asymptomatic</p>

Osterman 2021(b) (Continued)

(1) + (2) 256/445 (58%) PCR+ primary diagnosis, and 189/445 (42%) follow-up testing
Demographics: only reported for PCR- at site 1: 326/386 (84%) adults; 60/386 (16%) children
Exposure history: not mentioned

Index tests

Test name: STANDARD F COVID-19 Ag FIA
Manufacturer: SD Biosensor
Ag target: both nucleocapsid
Test method: FIA
Samples used: site (2) 66 NP; both collected by HCWs
Transport media: site (2) REST combi swabs (Nobel Bioscience, Sinbaek-gil, Republic of Korea) containing 2 mL of UTM
Sample storage: same day; site (2) PCR and Ag testing (RAT) were performed on the day of submission of freshly obtained swabs
Test operator: laboratory personnel according to manufacturer IFU
Definition of test positivity: a cut-off index (COI) ≥ 1 was interpreted as positive after 30 min
Blinding reported: not mentioned
Timing of samples: not mentioned

Target condition and reference standard(s)

Reference standard: PCR; multiple assays used at both sites
Definition of non-COVID cases:
Genetic target(s): site 2: N and RdRp gene
Samples used: as for index test; site 2: NP
Timing of reference standard: not mentioned
Blinded to index test: not mentioned
Incorporated index test: no

Flow and timing

Time interval between index and reference tests: assumed same time
All participants received same reference standard: all received PCR but many types/brands of PCR listed
Missing data: number PCR+ across the 2 sites sums to 447 but maximum number PCR+ reported was 445 (test [B]); only 381 reported for RAT test (site 1)
Uninterpretable results: none mentioned
Indeterminate results (index test): none mentioned
Indeterminate results (reference standard): none mentioned
Unit of analysis: participant

Comparative

Notes

Funding: "Open Access funding enabled and organized by Projekt DEAL. This work was supported in part by the German BMBF initiative "NaFoUniMedCovid19" (01KX2021), subproject

Osterman 2021(b) (Continued)

B-FAST (to U.P. and O.T.K.), and by the Medical Faculty of the LMU München, Munich, Germany (to O.T. K.)"

Publication status: published

Source: Medical Microbiology and Immunology

Author COI: the authors declare that they have 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Osterman 2021(b) *(Continued)*

Reference standard does not incorporate result of index test? Yes

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

Unclear risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Unclear risk

Parada-Ricart 2020
Study characteristics

Patient Sampling

Single-group study to estimate sensitivity and specificity.

Participants were patients with respiratory symptoms of < 7 days (128) and asymptomatic patients (44)

Recruitment: not mentioned

Prospective or retrospective: prospective

Sample size (cases): 193; final PCR diagnosis available for 172 (26 cases)

Patient characteristics and setting

Setting: unclear

Location: not mentioned. Author affiliations list Hospital Universitari de Tarragona JoanXXIII and Rovira i Virgili University

Country: Spain

Dates: 6-17 April 2020

Symptoms and severity: 128 with respiratory symptoms; no further details

Demographics: not mentioned

Parada-Ricart 2020 (Continued)

	Exposure history: not mentioned
Index tests	<p>Test name: SARS-CoV-2 (2019-n-CoV Ag Test Fluorescence IC Assay)</p> <p>Manufacturer: Shenzhen Bioeasy Biotechnology Co LTD</p> <p>Antibody: nucleocapsid</p> <p>Ag target:</p> <p>Test method: FIA</p> <p>Samples used: nasal; collection not reported</p> <p>Transport media: not mentioned</p> <p>Sample storage: none (tested within 30 min)</p> <p>Test operator: not mentioned</p> <p>Definition of test positivity: as per manufacturer IFU</p> <p>Blinding reported: not mentioned; but assume yes as tested within 30 min of collection</p> <p>Timing of samples: < 7 days pso</p>
Target condition and reference standard(s)	<p>Reference standard: PCR; not described</p> <p>Definition of non-COVID cases: single negative PCR, apart from discrepant cases (FPs) which were analysed by assessing clinical/radiology, previous/subsequent PCR results and serological data if available.</p> <p>Genetic target(s): not mentioned</p> <p>Samples used: nasal</p> <p>Timing of reference standard: < 7 days pso</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: different samples but same day</p> <p>All participants received same reference standard: yes</p> <p>Missing data: PCR result not available for 21 patients so not included in the analysis</p> <p>Uninterpretable results: not mentioned</p> <p>Indeterminate results (index test): not mentioned</p> <p>Indeterminate results (reference standard): not mentioned. Of 21 FPs, 13 remained after consideration of clinical history (9 asymptomatic and 4 symptomatic with negative subsequent serology); the remaining 8 were reclassified as TP (clinical-epidemiological picture compatible with COVID-19)</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	Funding: "partially funded by a call from the Department of Health of the Generalitat de Catalunya, code 6-17, main researcher: Francesc Vidal"

Parada-Ricart 2020 (Continued)

Publication status: published

Source: Enfermedades Infecciosas y Microbiología Clínica

Author COI: none 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

Parada-Ricart 2020 (Continued)

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

High risk

Pena 2021
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity: asymptomatic individuals at 7 testing sites, including workers (n = 56), "sanitary residence" [presumed to be health-related residential care] (n = 239), and the general public (n = 547); community prevalence of COVID-19 was 11%.

Recruitment: unclear

Prospective or retrospective: unclear

Sample size (cases): 854 included; 842 analysed (73)

Patient characteristics and setting

Setting: states "seven testing sites"; community screening

Location: Iquique city, Tarapacá Region

(Author institution: Laboratorio de Virología Molecular y Celular, Programa de Virología, Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad de Chile)

Country: Chile

Dates: 14-17 January 2021

Symptoms and severity: all asymptomatic (100%)

Demographics: mean age 36.67 (SD 16.48) years; 351 (42%) female

Exposure history: no details

Index tests

Test name: STANDARD Q COVID-19 Ag (catalogue number 9901-NCOV-01G)

Manufacturer: SD Biosensor, Inc. Republic of Korea

Antibody: not stated

Ag target: not stated

Pena 2021 (Continued)

	Test method: LFA chromatographic Samples used: NP (HCW collected) Transport media: none required (analysed according to the manufacturer IFU) Sample storage: none required (analysed according to the manufacturer IFU) Test operator: not stated but implies HCW at time of sampling Definition of test positivity: visual, coloured bands Blinding reported: yes (performed before PCR) Timing of samples: all described as asymptomatic; participants were asked about any symptoms in previous 0-14 days, but no information on responses was reported
Target condition and reference standard(s)	Reference standard: PCR (GenomeCov19 Detection Kit ABM; Applied Biological Materials Inc, Canada, catalogue number G628.v2) Ct ≤ 40 considered positive for the N and S viral gene Definition of non-COVID cases: N/A Genetic target(s): N and S gene Samples used: NP (analysed within 24–72 h of collection) Timing of reference standard: as for index test Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired swabs All participants received same reference standard: yes Missing data: yes; 12 (1.4%) were excluded for lacking real-time PCR results Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: Funded by Ministerio de Salud de Chile Publication status: preprint Source: medRxiv Author COI: "the authors are supported by ANID Chile through Fondecyt grants"

Methodological quality

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

Pena 2021 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pena 2021 (Continued)

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

Pena-Rodriguez 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: adults with symptoms suggestive of COVID-19 (headache, fever, fatigue, other respiratory signs, or gastrointestinal symptoms) and individuals in contact with confirmed cases of COVID-19 (by RT-PCR) in the previous 3-5 days, with or without symptoms attending for COVID-19 testing</p> <p>Recruitment: unclear</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 369 (104)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre (diagnostic laboratory centre)</p> <p>Location: Guadalajara (Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara)</p> <p>Country: Mexico</p> <p>Dates: October-November 2020</p> <p>Symptoms and severity: symptoms included: headache (42%), fever (25%), cough (23%), myalgia (21%), loss of smell (18%), fatigue (16%), diarrhoea (10%), shortness of breath (7%), arthralgia (4%)</p> <p>Demographics: average age 36.6 ± 13.16 years; 215 (58%) female</p> <p>Exposure history: individuals in contact with confirmed cases of COVID-19 in the last 3-5 days included; no further details</p>
Index tests	<p>Test name: STANDARD Q COVID-19</p> <p>Manufacturer: SD BIOSENSOR</p> <p>Antibody: N gene</p> <p>Ag target: not stated</p> <p>Test method: chromatographic</p> <p>Samples used: NP; single nostril (collected by "trained staff")</p> <p>Transport media: not used</p> <p>Sample storage: none; "SARS-CoV-2 antigen analysis was carried out in the place"</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pena-Rodriguez 2021 (Continued)

	Test operator: trained staff Definition of test positivity: visual control and test lines The test was invalidated when no marks were detected Blinding reported: yes; performed before PCR) Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR; DeCoV19 Kit Triplex (Genes2life SAPI de CV, Mexico) Ct < 35 with an exponential growth curve of ≥ 2 genes were considered as positive Definition of non-COVID cases: same as for cases (single -ve PCR) Genetic target(s): N gene and Rnase P gene (RP) Samples used: combined NP/OP in VTM Timing of reference standard: same as for index test Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported; States "The test was invalidated when no marks were detected" Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: P.M.I 12.10, SAPI de CV, grant/award Number: 251472 Publication status: published Source: Journal of Clinical Laboratory Analysis Author COI: RAT was "supplied by PMI 12.10, SAPI de CV company" [appears to be a medical supplies company which imports the SD Biosensor assay]. No other 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?	Unclear		
Was a case-control design avoided?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pena-Rodriguez 2021 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pena-Rodriguez 2021 (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Perez-Garcia 2021 [A]
Study characteristics

Patient Sampling 2-group study to estimate sensitivity and specificity: samples from patients with suspicion of COVID-19 attending the university hospital or associated primary healthcare centres
 1] PCR-ve patients (n = 150)
 2] PCR+ve patients (n = 170)

Recruitment: not stated; appears to be deliberate sampling based on PCR status

Prospective or retrospective: retrospective

Sample size (cases): 320 (170)

Patient characteristics and setting Setting: laboratory-based; samples from mixed settings including primary healthcare centres (50%), hospital inpatients (20%), ED (21%) and occupational health (9%)

Location: Madrid (Servicio de Microbiología Clínica, Hospital Universitario Príncipe de Asturias, Madrid)

Country: Spain

Dates: 8-20 October 2020

Symptoms and severity: 134 (79%) symptomatic; including cough (54%), fever (41%), dyspnoea (25%), anosmia (22%) and myalgia (19%); 26 (15%) asymptomatic with a prior contact with COVID-19 case

Demographics: median age 51 years (IQR: 38-68); (10 with no data on symptoms; time pso not reported for 6/134 symptomatic)

81 (48%) female

Exposure history: states "26 (15%) asymptomatic with a prior contact with COVID-19 case"; no further details

Index tests Test name:

[A] CerTest SARS-CoV-2 Ag One Step Card Test (Batch code SC-004)
 [B] Panbio COVID-19 Ag Rapid Test Device (Batch code 41ADF057A)

Manufacturer:

[A] Certest Biotec S.L., Zaragoza, Spain
 [B] Abbot Rapid Diagnostics GmbH, Jena, Germany

Antibody: both nucleoprotein antigens

Ag target: not stated

Test method: **[A] LFA**; [B] CGIA

Samples used: residual NP swabs in VTM

Perez-Garcia 2021 [A] (Continued)

Transport media: 3 mL of UTM (Vircell, SL, Granada, Spain, or Deltalab, Barcelona, Spain)

Sample storage: samples were cryopreserved at -20 °C until their analysis by Ag-RDTs

Test operator: not stated (lab-based)

Definition of test positivity: visual; control and test lines

Blinding reported: unclear

Timing of samples: reported for 128 PCR+ samples: 46 (36%) < 5 days pso; 55 (43%) day 6-10; 27 (21%) > 10 days

Target condition and reference standard(s)

Reference standard: RT-PCR performed using either of the following:

1. Viasure SARS-CoV-2 Real Time PCR Detection Kit (Certest Biotech S.L., Zaragoza, Spain) (batch code NCO212L-170)
2. Allplex SARS-CoV-2 assay (Seegene, Seoul South Korea) (batch code RV9120G16)
3. GeneFinder COVID-19 Plus RealAmp Kit (Osang Healthcare Co., Gyeonggi, South Korea)
4. (batch code 2004-R45-19)

All target genes present per assay

Definition of non-COVID cases: single negative

Genetic target(s):

1. ORF1ab and N genes
2. E, RdRP, S and N
3. E, RdRP and N

Samples used: NP samples (processed upon arrival at the laboratory)

Timing of reference standard: as for index test

Blinded to index test: yes (processed upon arrival at the laboratory before Ag test)

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: funded by Certest Biotech S.L. (Zaragoza, Spain); Each manufacturer provided Panbio and CerTest devices.

Publication status: published

Source: Journal of Clinical Virology

Author COI: the authors report no COI

Perez-Garcia 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

Perez-Garcia 2021 [A] *(Continued)*

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Unclear risk

Perez-Garcia 2021 [B]
Study characteristics

Patient Sampling Comparative study of 2 Ag tests; [Perez-Garcia 2021 \[A\]](#) details the full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 2 Ag tests; [Perez-Garcia 2021 \[A\]](#) details the full study characteristics and QUADAS.

Index tests Test name: [A] CerTest SARS-CoV-2 Ag One Step Card Test (Batch code SC-004) **[B] Panbio COVID-19 Ag Rapid Test Device (Batch code 41ADF057A)**

Manufacturer: [A] Certest Biotec S.L., Zaragoza, Spain **[B] Abbot Rapid Diagnostics GmbH, Jena, Germany**

Antibody: both nucleoprotein antigens

Ag target: not stated

Test method: [A] LFA; **[B] CGIA**

Samples used: residual NP swabs in VTM

Transport media: 3 mL of UTM (Viracell, SL, Granada, Spain, or Deltalab, Barcelona, Spain)

Sample storage: samples were cryopreserved at -20 °C until their analysis by Ag-RDTs

Test operator: not stated (lab-based)

Definition of test positivity: visual; control and test lines

Blinding reported: unclear

Timing of samples: reported for 128 PCR+ samples: 46 (36%) < 5 days pso; 55 (43%) day 6-10; 27 (21%) > 10 days

Perez-Garcia 2021 [B] *(Continued)*

Target condition and reference standard(s) Comparative study of 2 Ag tests; [Perez-Garcia 2021 \[A\]](#) details the full study characteristics and QUADAS.

Flow and timing Comparative study of 2 Ag tests; [Perez-Garcia 2021 \[A\]](#) details the full study characteristics and QUADAS.

Comparative

Notes Comparative study of 2 Ag tests; [Perez-Garcia 2021 \[A\]](#) details the full study characteristics and QUADAS.

Peto 2021(a) [A]
Study characteristics

Patient Sampling Set of studies conducted by PHE and University of Oxford. This extraction relates to a 2-group study estimating sensitivity and specificity (Phase 3a):
 [1] residual frozen swabs from PCR+ patients in Oxford (collected March 2020)
 [2] residual fresh swabs from PCR- patients in Oxford (collected March 2020)
 Swabs were frozen following routine testing and sent to Porton Down
 See other PHE extractions for other substudies of Innova assay

Recruitment: unclear

Prospective or retrospective: retrospective

Sample size (cases): 1118 (178)

Patient characteristics and setting Setting: inpatient; obtained from a secondary healthcare setting (cases described as from patients admitted to hospital)

Location: John Radcliffe Hospital, Oxford (Ag testing at PHE Porton Down)

Country: UK

Dates: March 2020 (PCR+)

Symptoms and severity: not stated

Demographics: not stated

Exposure history: not stated

Index tests Comparative study of 7 Ag tests (no product codes reported); [Peto 2021\(a\) \[A\]](#) data relate to test [A], see additional entries for tests [B] to [G]

Test name:

[A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test

[B] Panbio COVID-19 Ag Rapid Test Device

[C] Coronavirus Ag Rapid Test Cassette

[D] Anhui Deepblue Medical Technology COVID-19

[E] Fortress Diagnostics Coronavirus Ag Rapid Test

[F] STANDARD Q COVID-19 Ag Test

[G] Surescreen Diagnostics SARS-CoV-2 Antigen Rapid Test Cassette

Manufacturer:

[A] Innova Medical Group

[B] Abbott

[C] Zhejiang Orient Gene Biotech

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Peto 2021(a) [A] (Continued)

[D] Deepblue
 [E] Fortress
 [F] SD Biosensor
 [G] Surescreen

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: NP and OP swabs

Transport media: VTM (1 mL)

Sample storage: frozen (PCR+); fresh (PCR-)

Test operator: laboratory staff

Definition of test positivity: visual line; as per manufacturer IFU

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: RT-PCR; from preprint "Viral load (in RNA copies/mL) was quantified from Ct values by using a conversion factor obtained using a dilution calibration series of synthetic genomic RNA (Twist Bioscience) and a standard curve performed using Altona and Taqpath ORF and S target assays. Viral load conversion to RNA copies/mL was performed using the following equation derived from prior calibration curves, $\log_{10} VL = 11.19 - 0.304 * (\Delta CT - 4.4)$." Published version further states: "In order to compare the sensitivity of Phase 3a with Phase 3b the Phase 3a viral loads were reduced by $\log_{10}(2000/300) = 0.82$ log units."

Definition of non-COVID cases: single negative PCR

Genetic target(s): ORF and S target assays

Samples used: appears to be same sample as for Ag test

Timing of reference standard: as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab

All participants received same reference standard: yes

Missing data: see below, plus 1 void PCR

Uninterpretable results: failure rates reported for test [A] only:
 [1] 13/191, 7%
 [2] 50/990, 5.1%

Indeterminate results (index test): unclear

Indeterminate results (reference standard): unclear

Unit of analysis: participant

Comparative
Notes

Funding: "the report presents independent research funded by the NIHR, Wellcome Trust and the Department of Health."

Peto 2021(a) [A] (Continued)

Publication status: published

Source: EClinicalMedicine

Author COI: the authors do not have any conflicts of interest

Publication status: published

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Peto 2021(a) [A] *(Continued)*

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Peto 2021(a) [B]
Study characteristics

Patient Sampling Comparative study of 7 Ag tests (no product codes reported); [Peto 2021\(a\) \[A\]](#) reports full study characteristics and QUADAS

Patient characteristics and setting Comparative study of 7 Ag tests (no product codes reported); [Peto 2021\(a\) \[A\]](#) reports full study characteristics and QUADAS

Index tests Comparative study of 7 Ag tests (no product codes reported); [Peto 2021\(a\) \[B\]](#) data relate to test [B], see additional entries for other tests

Test name:

[A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test

[B] Panbio COVID-19 Ag Rapid Test Device

[C] Coronavirus Ag Rapid Test Cassette

[D] Anhui Deepblue Medical Technology COVID-19

[E] Fortress Diagnostics Coronavirus Ag Rapid Test

[F] STANDARD Q COVID-19 Ag Test

[G] Surescreen Diagnostics SARS-CoV-2 Antigen Rapid Test Cassette

Manufacturer:

[A] Innova Medical Group

[B] Abbott

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Peto 2021(a) [B] *(Continued)*

[C] Zhejiang Orient Gene Biotech
 [D] Deepblue
 [E] Fortress
 [F] SD Biosensor
 [G] Surescreen

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: NP and OP swabs

Transport media: VTM (1 mL)

Sample storage: frozen (PCR+); fresh (PCR-)

Test operator: laboratory staff

Definition of test positivity: visual line; as per manufacturer IFU

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Comparative

Notes

Peto 2021(a) [C]
Study characteristics

Patient Sampling	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Patient characteristics and setting	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Index tests	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [C] data relate to test [C], see additional entries for other tests
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Test name:

[A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test
 [B] Panbio COVID-19 Ag Rapid Test Device
[C] Coronavirus Ag Rapid Test Cassette
 [D] Anhui Deepblue Medical Technology COVID-19
 [E] Fortress Diagnostics Coronavirus Ag Rapid Test
 [F] STANDARD Q COVID-19 Ag Test
 [G] Surescreen Diagnostics SARS-CoV-2 Antigen Rapid Test Cassette

Peto 2021(a) [C] (Continued)

Manufacturer:

- [A] Innova Medical Group
- [B] Abbott
- [C] Zhejiang Orient Gene Biotech**
- [D] Deepblue
- [E] Fortress
- [F] SD Biosensor
- [G] Surescreen

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: NP and OP swabs

Transport media: VTM (1 mL)

Sample storage: frozen (PCR+); fresh (PCR-)

Test operator: laboratory staff

Definition of test positivity: visual line; as per manufacturer IFU

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Comparative

Notes

Peto 2021(a) [D]

Study characteristics

Patient Sampling	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Patient characteristics and setting	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Index tests	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [D] data relate to test [D], see additional entries for other tests
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Test name:

- [A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test
- [B] Panbio COVID-19 Ag Rapid Test Device
- [C] Coronavirus Ag Rapid Test Cassette
- [D] Anhui Deepblue Medical Technology COVID-19**

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Peto 2021(a) [D] *(Continued)*

- [E] Fortress Diagnostics Coronavirus Ag Rapid Test
- [F] STANDARD Q COVID-19 Ag Test
- [G] Surescreen Diagnostics SARS-CoV-2 Antigen Rapid Test Cassette

Manufacturer:

- [A] Innova Medical Group
- [B] Abbott
- [C] Zhejiang Orient Gene Biotech
- [D] Deepblue**
- [E] Fortress
- [F] SD Biosensor
- [G] Surescreen

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: NP and OP swabs

Transport media: VTM (1 mL)

Sample storage: frozen (PCR+); fresh (PCR-)

Test operator: laboratory staff

Definition of test positivity: visual line; as per manufacturer IFU

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Comparative	
Notes	

Peto 2021(a) [E]
Study characteristics

Patient Sampling	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Index tests	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [E] data relate to test [E], see additional entries for other tests
	Test name:

Peto 2021(a) [E] *(Continued)*

- [A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test
- [B] Panbio COVID-19 Ag Rapid Test Device
- [C] Coronavirus Ag Rapid Test Cassette
- [D] Anhui Deepblue Medical Technology COVID-19
- [E] Fortress Diagnostics Coronavirus Ag Rapid Test**
- [F] STANDARD Q COVID-19 Ag Test
- [G] Surescreen Diagnostics SARS-CoV-2 Antigen Rapid Test Cassette

Manufacturer:

- [A] Innova Medical Group
- [B] Abbott
- [C] Zhejiang Orient Gene Biotech
- [D] Deepblue
- [E] Fortress**
- [F] SD Biosensor
- [G] Surescreen

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: NP and OP swabs

Transport media: VTM (1 mL)

Sample storage: frozen (PCR+); fresh (PCR-)

Test operator: laboratory staff

Definition of test positivity: visual line; as per manufacturer IFU

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Comparative	
Notes	

Peto 2021(a) [F]
Study characteristics

Patient Sampling	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS

Peto 2021(a) [F] (Continued)

Index tests	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [F] data relate to test [F], see additional entries for other tests Test name: [A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test [B] Panbio COVID-19 Ag Rapid Test Device [C] Coronavirus Ag Rapid Test Cassette [D] Anhui Deepblue Medical Technology COVID-19 [E] Fortress Diagnostics Coronavirus Ag Rapid Test [F] STANDARD Q COVID-19 Ag Test [G] Surescreen Diagnostics SARS-CoV-2 Antigen Rapid Test Cassette Manufacturer: [A] Innova Medical Group [B] Abbott [C] Zhejiang Orient Gene Biotech [D] Deepblue [E] Fortress [F] SD Biosensor [G] Surescreen Antibody: not stated Ag target: not stated Test method: not stated Samples used: NP and OP swabs Transport media: VTM (1 mL) Sample storage: frozen (PCR+); fresh (PCR-) Test operator: laboratory staff Definition of test positivity: visual line; as per manufacturer IFU Blinding reported: not stated Timing of samples: not stated
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Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
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 Comparative

 Notes

Peto 2021(a) [G]
Study characteristics

Peto 2021(a) [G] (Continued)

Patient Sampling	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Index tests	<p>Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [G] data relate to test [G], see additional entries for other tests</p> <p>Test name:</p> <p>[A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test [B] Panbio COVID-19 Ag Rapid Test Device [C] Coronavirus Ag Rapid Test Cassette [D] Anhui Deepblue Medical Technology COVID-19 [E] Fortress Diagnostics Coronavirus Ag Rapid Test [F] STANDARD Q COVID-19 Ag Test [G] Surescreen Diagnostics SARS-CoV-2 Antigen Rapid Test Cassette</p> <p>Manufacturer:</p> <p>[A] Innova Medical Group [B] Abbott [C] Zhejiang Orient Gene Biotech [D] Deepblue [E] Fortress [F] SD Biosensor [G] Surescreen</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP and OP swabs</p> <p>Transport media: VTM (1 mL)</p> <p>Sample storage: frozen (PCR+); fresh (PCR-)</p> <p>Test operator: laboratory staff</p> <p>Definition of test positivity: visual line; as per manufacturer IFU</p> <p>Blinding reported: not stated</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(a) [A] reports full study characteristics and QUADAS
Comparative	
Notes	

Peto 2021(b) [non-HCW tested]

Study characteristics

Patient Sampling	<p>Set of studies conducted by PHE and University of Oxford. This extraction relates to a single-group study estimating sensitivity and specificity: individuals presenting at a regional COVID-19 testing centre as part of a Phase 4 community field service evaluation (n = 1946; according to Table 3 of preprint) See other PHE extractions for other sub-studies of Innova assay</p> <p>Recruitment: not stated; presume consecutive</p> <p>Prospective or retrospective: not stated</p>
Patient characteristics and setting	<p>Setting: regional COVID-19 testing centres as part of an NHS Test and Trace service evaluation involving the general public</p> <p>Location: not stated</p> <p>Country: UK</p> <p>Dates: not stated</p> <p>Symptoms and severity: not stated, presumed 'mainly symptomatic ' for purposes of review analyses</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Innova SARS-CoV-2 Antigen Rapid Qualitative Test</p> <p>Manufacturer: Innova Medical Group</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: AN and combined oropharyngeal samples</p> <p>Transport media: dry swab</p> <p>Sample storage: none; immediate testing</p> <p>Test operator: self-trained non-HCW ('Boots' member of staff); described in preprint as an "operator" or as "self-trained members of the public".</p> <p>Definition of test positivity: visual line; as per manufacturer IFU</p> <p>Blinding reported: yes; conducted on site</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: PCR; no details. The preprint supplementary materials describes using the "Roche platform" under the Phase 3b heading, and also provides the following text under the Phase 2 evaluation heading "Unless otherwise stated, all PCR testing was undertaken on the Roche Cobas 6800 or 8800 system using their proprietary SARS-CoV-2 assay as per manufacturer IFU (with off-board lysis using AVL buffer (Qiagen) and 5% Triton-X100 (Sigma Aldrich)). This assay detects ORF-1a/b as a SARS-CoV-2 specific target, and the E-gene as a pan-sarbecovirus target."</p> <p>Definition of non-COVID cases: N/A; cases-only study</p>

Peto 2021(b) [non-HCW tested] (Continued)

Genetic target(s): not stated

Samples used: not stated; paired swabs obtained

Timing of reference standard: as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired swabs; simultaneous

All participants received same reference standard: yes

Missing data: initial sample of 1946 reported, 27 failed, leaving 1919 for inclusion, however data for only 1676 samples are provided in the published study (1314 PCR- in Table 3 and 372 PCR+ in text pg 7), a difference of 243 samples.

Uninterpretable results: failure rate reported as 27/1946 failed, 1.4%

Indeterminate results (index test): unclear

Indeterminate results (reference standard): unclear

Unit of analysis: participant

Comparative
Notes

Funding: PHE evaluation

Publication status: published

Source: online PHE report

Author COI: none 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 inclusions?	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 (Evaluations of single test application)			

Peto 2021(b) [non-HCW tested] *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Peto 2021(c) [A - HCW tested]
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Peto 2021(c) [A - HCW tested] (Continued)

Patient Sampling	<p>Set of studies conducted by PHE and University of Oxford. This extraction relates to a single-group study estimating sensitivity alone: individuals presenting at one of 14 regional drive-through COVID-19 NHS Test and Trace centres as part of the FALCON C-19 (Facilitating Accelerated Clinical validation Of Novel diagnostics for COVID-19, 20/WA/0169, IRAS 284229) phase 3b study; those with a positive PCR result were asked to return for a re-test within 5 days of the original test result. From the originally published report (November 2020) it appears that only participants with samples that were positive on PCR at the second sampling were included.</p> <p>(1) One set of samples were tested on site by HCWs using assay [A] only: n = 267; included as Peto 2021(c) [A - HCW tested]</p> <p>(2) Second set of samples were tested in the laboratory by laboratory scientists using four different assays [A] to [D]: n = 212; included as Peto 2021(c) [A - Lab tested], Peto 2021(c) [B - Lab tested], Peto 2021(c) [C - Lab tested], Peto 2021(c) [D - Lab tested]</p> <p>Recruitment: not stated; presume consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Number of samples (cases): 479 (479)</p>
Patient characteristics and setting	<p>Setting: NHS drive-through Test and Trace centres; conducted within the FALCON-C19 study</p> <p>Location: 14 regional centres</p> <p>Country: UK</p> <p>Dates: 17 September-23 October 2020</p> <p>Symptoms and severity: only described for 421 included participants combined: 381 (90%) symptomatic; 138 (36%) headache, 134 (35%) cough, 82 (22%) sore throat, 80 (21%) fever, 260 (68%) 'other' not specified symptoms, 59 with no data. 40 (10%) reported asymptomatic</p> <p>Demographics: not stated median age 33 (91 with no data); 168/337 male, 50% (84 with no data recorded)</p> <p>Exposure history: not stated</p>
Index tests	<p>Comparative study of 4 Ag tests (no product codes reported); Peto 2021(c) [A - HCW tested] and Peto 2021(c) [A - Lab tested] data relate to test [A], see additional entries for tests [B] to [D]</p> <p>Test name:</p> <p>[A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test [B] Panbio COVID-19 Ag Rapid Test Device [C] Coronavirus Ag Rapid Test Cassette [D] Anhui Deepblue Medical Technology COVID-19</p> <p>Manufacturer:</p> <p>[A] Innova Medical Group [B] Abbott [C] Zhejiang Orient Gene Biotech [D] Deepblue</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: combined AN and OP swabs (1 stored as a dry swab and 1 swab placed in VTM; swabs were self-collected)</p>

Peto 2021(c) [A - HCW tested] *(Continued)*

Transport media: dry swab

Sample storage:

- (1) immediate on-site testing by HCW
- (2) transport to PHE; tested within 24 h of collection

Test operator:

- (1) Immediate testing by HCW (assay [A])
- (2) laboratory scientist tested at PHE (assay [A] to [D])

Definition of test positivity: visual line; as per manufacturer IFU

An invalid kit result, or a kit failure was recorded when an operator did not see a control line on the device within a defined time period

Blinding reported: yes for on-site HCW testing; lab scientists reported as unaware of clinical information from the study participants

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: PCR; Roche Cobas 6800 or 8800 system using their proprietary SARS-CoV-2 assay

Viral load conversion to RNA copies/mL was performed using the Qnostics SARS-CoV-2 Analytical Q Panel 01 (Qnostics, Glasgow, UK); the resulting equation for converting Ct values into viral loads for the Cobas assay, included an adjustment for the dilution, was $\log_{10}(VL) = 14.17 - 0.3316 * avct$

Definition of non-COVID cases: N/A; cases-only study

Genetic target(s): ORF-1 and E-gene

Samples used: AN + OP

Timing of reference standard: as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired

All participants received same reference standard: yes

Missing data: yes; appears that only those who remained PCR+ on return for Ag testing were included (the original report (November 2020) documented 16 HCW-tested samples that were either PCR -ve (n = 15) or void (n = 1) presumably at the time of the second sampling (partially explains discrepancy in numbers)

Uninterpretable results: failure rates reported for assay [A] only as: HCW tested 27/267 10.1%; lab scientist tested 9/212 4.2%. NB preliminary report reported these as 28/296 and 9/221 respectively

Indeterminate results (index test): unclear

Indeterminate results (reference standard): unclear

Unit of analysis: participant

Comparative

Notes

Funding: PHE evaluation

Publication status: published

Peto 2021(c) [A - HCW tested] *(Continued)*

Source: online PHE report; published paper

Author COI: none 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without	Unclear		

Peto 2021(c) [A - HCW tested] *(Continued)*

knowledge of the results of the index tests?

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? No

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Peto 2021(c) [A - Lab tested]
Study characteristics

Patient Sampling Set of studies conducted by PHE and University of Oxford. This extraction relates to a single-group study estimating sensitivity alone: individuals presenting at 1 of 14 regional drive-through COVID-19 NHS Test and Trace centres as part of the FALCON C-19 (Facilitating Accelerated Clinical validation Of Novel diagnostics for COVID-19, 20/WA/0169, IRAS 284229) phase 3b study; those with a positive PCR result were asked to return for a re-test within 5 days of the original test result. From the originally published report (November 2020) it appears that only participants with samples that were positive on PCR at the second sampling were included.

(1) One set of samples were tested on site by HCWs using assay [A] only: n = 267; included as [Peto 2021\(c\) \[A - HCW tested\]](#)

(2) Second set of samples were tested in the laboratory by laboratory scientists using four different assays [A] to [D]: n = 212; included as [Peto 2021\(c\) \[A - Lab tested\]](#), [Peto 2021\(c\) \[B - Lab tested\]](#), [Peto 2021\(c\) \[C - Lab tested\]](#), [Peto 2021\(c\) \[D - Lab tested\]](#)

See other PHE extractions for other sub-studies of Innova assay

Recruitment: not stated; presume consecutive

Peto 2021(c) [A - Lab tested] (Continued)

Prospective or retrospective: prospective

Number of samples (cases): 479 (479)

Patient characteristics and setting

Setting: NHS drive through Test and Trace centres; conducted within the FALCON-C19 study

Location: 14 regional centres

Country: UK

Dates: 17 Sept to 23 Oct 2020

Symptoms and severity: only described for 421 included participants combined: 381 (90%) symptomatic; 138 (36%) headache, 134 (35%) cough, 82 (22%) sore throat, 80 (21%) fever, 260 (68%) 'other' not specified symptoms, 59 with no data.

40 (10%) reported asymptomatic

Demographics: median age 33 (91 with no data); 168/337 male, 50% (84 with no data recorded)

Exposure history: not stated

Index tests

Comparative study of 4 Ag tests (no product codes reported); [Peto 2021\(c\) \[A - HCW tested\]](#) and [Peto 2021\(c\) \[A - Lab tested\]](#) data relate to test [A], see additional entries for tests [B] to [D]

Test name:

[A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test

[B] Panbio COVID-19 Ag Rapid Test Device

[C] Coronavirus Ag Rapid Test Cassette

[D] Anhui Deepblue Medical Technology COVID-19

Manufacturer:

[A] Innova Medical Group

[B] Abbott

[C] Zhejiang Orient Gene Biotech

[D] Deepblue

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: combined AN and OP swabs (1 stored as a dry swab and 1 swab placed in VTM; swabs were self-collected)

Transport media: dry swab

Sample storage:

(1) immediate on-site testing by HCW

(2) transport to PHE; tested within 24 h of collection

Test operator:

(1) Immediate testing by HCW (assay [A])

(2) laboratory scientist tested at PHE (assay [A] to [D])

Definition of test positivity: visual line; as per manufacturer IFU

An invalid kit result, or a kit failure was recorded when an operator did not see a control line on the device within a defined time period

Peto 2021(c) [A - Lab tested] *(Continued)*

	Blinding reported: yes for on-site HCW testing; lab scientists reported as unaware of clinical information from the study participants Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: PCR; Roche Cobas 6800 or 8800 system using their proprietary SARS-CoV-2 assay Viral load conversion to RNA copies/mL was performed using the Qnostics SARS-CoV-2 Analytical Q Panel 01 (Qnostics, Glasgow, UK); the resulting equation for converting Ct values into viral loads for the Cobas assay, included an adjustment for the dilution, was $\log_{10}(\text{VL}) = 14.17 - 0.3316 \cdot \text{avct}$ Definition of non-COVID cases: N/A; cases-only study Genetic target(s): ORF-1 and E-gene Samples used: AN + OP Timing of reference standard: as for index test Blinded to index test: not stated Incorporated index test: no
Flow and timing	Time interval between index and reference tests: paired All participants received same reference standard: yes Missing data: yes; appears that only those who remained PCR+ on return for Ag testing were included (the original report (November 2020) documented 16 HCW-tested samples that were either PCR -ve (n = 15) or void (n = 1) presumably at the time of the second sampling (partially explains discrepancy in numbers) Uninterpretable results: failure rates reported for assay [A] only as: HCW tested 27/267 10.1%; lab scientist tested 9/212 4.2%. NB preliminary report reported these as 28/296 and 9/221 respectively Indeterminate results (index test): unclear; Indeterminate results (reference standard): unclear Unit of analysis: participant
Comparative	
Notes	Funding: PHE evaluation Publication status: published Source: online PHE report; published paper Author COI: none 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		

Peto 2021(c) [A - Lab tested] (Continued)

Was a case-control design avoided? No

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

Are there concerns that the target condition as defined High

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Peto 2021(c) [A - Lab tested] *(Continued)*
**by the reference standard
 does not match the ques-
 tion?**

DOMAIN 4: Flow and Timing

Was there an appropriate in-
 terval between index test and
 reference standard? No

Did all patients receive the
 same reference standard? Yes

Were all patients included in
 the analysis? No

Did all participants receive a
 reference standard? Yes

**Could the patient flow have
 introduced bias?** High risk

Peto 2021(c) [B - Lab tested]

Study characteristics

Patient Sampling Comparative study of 4 Ag tests (no product codes reported); [Peto 2021\(c\) \[A - Lab tested\]](#) reports full study characteristics and QUADAS

Patient characteris-
 tics and setting Comparative study of 4 Ag tests (no product codes reported); [Peto 2021\(c\) \[A - Lab tested\]](#) reports full study characteristics and QUADAS

Index tests Comparative study of 4 Ag tests (no product codes reported); [Peto 2021\(c\) \[B - Lab tested\]](#) data relate to test [B], see additional entries for other assays

Test name:

[A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test
[B] Panbio COVID-19 Ag Rapid Test Device
 [C] Coronavirus Ag Rapid Test Cassette
 [D] Anhui Deepblue Medical Technology COVID-19

Manufacturer:

[A] Innova Medical Group
[B] Abbott
 [C] Zhejiang Orient Gene Biotech
 [D] Deepblue

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: combined AN and OP swabs (1 stored as a dry swab and 1 swab placed in VTM; swabs were self-collected)

Transport media: dry swab

Peto 2021(c) [B - Lab tested] (Continued)

Sample storage:

- (1) immediate on-site testing by HCW
- (2) transport to PHE; tested within 24 h of collection

Test operator:

- (1) Immediate testing by HCW (assay [A])
- (2) laboratory scientist tested at PHE (assay [A] to [D])

Definition of test positivity: visual line; as per manufacturer IFU

An invalid kit result, or a kit failure was recorded when an operator did not see a control line on the device within a defined time period

Blinding reported: yes for on-site HCW testing; lab scientists reported as unaware of clinical information from the study participants

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
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Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
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Comparative

Notes

Peto 2021(c) [C - Lab tested]

Study characteristics

Patient Sampling	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
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Patient characteristics and setting	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
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Index tests	Comparative study of 4 Ag tests (no product codes reported); Peto 2021(c) [C - Lab tested] data relate to test [C], see additional entries for other assays
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Test name:

- [A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test
- [B] Panbio COVID-19 Ag Rapid Test Device
- [C] Coronavirus Ag Rapid Test Cassette**
- [D] Anhui Deepblue Medical Technology COVID-19

Manufacturer:

- [A] Innova Medical Group
- [B] Abbott
- [C] Zhejiang Orient Gene Biotech**
- [D] Deepblue

Antibody: not stated

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Peto 2021(c) [C - Lab tested] *(Continued)*

Ag target: not stated

Test method: not stated

Samples used: combined AN and OP swabs (1 stored as a dry swab and 1 swab placed in VTM; swabs were self-collected)

Transport media: dry swab

Sample storage:

(1) immediate on-site testing by HCW

(2) transport to PHE; tested within 24 h of collection

Test operator:

(1) Immediate testing by HCW (assay [A])

(2) laboratory scientist tested at PHE (assay [A] to [D])

Definition of test positivity: visual line; as per manufacturer IFU

An invalid kit result, or a kit failure was recorded when an operator did not see a control line on the device within a defined time period

Blinding reported: yes for on-site HCW testing; lab scientists reported as unaware of clinical information from the study participants

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
Comparative	
Notes	

Peto 2021(c) [D - Lab tested]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
Patient characteristics and setting	Comparative study of 4 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
Index tests	Comparative study of 4 Ag tests (no product codes reported); Peto 2021(c) [D - Lab tested] data relate to test [D], see additional entries for other assays Test name: [A] Innova SARS-CoV-2 Antigen Rapid Qualitative Test [B] Panbio COVID-19 Ag Rapid Test Device [C] Coronavirus Ag Rapid Test Cassette [D] Anhui Deepblue Medical Technology COVID-19

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Peto 2021(c) [D - Lab tested] (Continued)

Manufacturer:

- [A] Innova Medical Group
- [B] Abbott
- [C] Zhejiang Orient Gene Biotech
- [D] Deepblue**

Antibody: not stated

Ag target: not stated

Test method: not stated

Samples used: combined AN and OP swabs (1 stored as a dry swab and 1 swab placed in VTM; swabs were self-collected)

Transport media: dry swab

Sample storage:

- (1) immediate on-site testing by HCW
- (2) transport to PHE; tested within 24 h of collection

Test operator:

- (1) Immediate testing by HCW (assay [A])
- (2) laboratory scientist tested at PHE (assay [A] to [D])

Definition of test positivity: visual line; as per manufacturer IFU

An invalid kit result, or a kit failure was recorded when an operator did not see a control line on the device within a defined time period

Blinding reported: yes for on-site HCW testing; lab scientists reported as unaware of clinical information from the study participants

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 4 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
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Flow and timing	Comparative study of 7 Ag tests (no product codes reported); Peto 2021(c) [A - Lab tested] reports full study characteristics and QUADAS
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Comparative

Notes

Peto 2021(d)

Study characteristics

Patient Sampling	Set of studies conducted by PHE and University of Oxford. This extraction relates to a single-group study estimating specificity alone: PHE and hospital staff volunteering for testing (n = 538) See other PHE extractions for other sub-studies of Innova assay Recruitment: not stated; presume consecutive
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Peto 2021(d) (Continued)

	Prospective or retrospective: not stated
Patient characteristics and setting	<p>Setting: screening</p> <p>Location: PHE and John Radcliffe Hospital, Oxford</p> <p>Country: UK</p> <p>Dates: not stated</p> <p>Symptoms and severity: not stated; hospital staff described as asymptomatic</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Innova SARS-CoV-2 Antigen Rapid Qualitative Test</p> <p>Manufacturer: Innova Medical Group</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: OP swab for PHE staff; NP swab for hospital staff. All self-collected</p> <p>Transport media: dry swab</p> <p>Sample storage: none; immediate testing</p> <p>Test operator: not stated; presumably laboratory scientist at PHE</p> <p>Definition of test positivity: visual line; as per manufacturer IFU</p> <p>Blinding reported: unclear</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; no details (single negative PCR OK for asymptomatic). The preprint supplementary materials describes using the "Roche platform" under the Phase 3b heading, and also provides the following text under the Phase 2 evaluation heading "Unless otherwise stated, all RT-PCR testing was undertaken on the Roche Cobas 6800 or 8800 system using their proprietary SARS-CoV-2 assay as per manufacturer IFU (with off-board lysis using AVL buffer (Qiagen) and 5% Triton-X100 (Sigma Aldrich)). This assay detects ORF-1a/b as a SARS-CoV-2 specific target, and the E-gene as a pan-sarbecovirus target."</p> <p>DGenetic target(s): not stated</p> <p>Samples used: not stated; presume same or paired swab</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: unclear, may have been a few days</p> <p>All participants received same reference standard: yes</p>

Peto 2021(d) (Continued)

Missing data: initial sample of 570 reported (358 hospital staff and 212 PHE staff), 36 failed (Table 4: 17 hospital staff and 19 PHE staff), leaving 534 for inclusion. Data for 538 included

Uninterpretable results: failure rate reported as 17/358, 4.7% (hospital) 19/212, 8.9% (PHE)

Indeterminate results (index test): unclear

Indeterminate results (reference standard): unclear

Unit of analysis: participant

Comparative

Notes

Funding: PHE evaluation

Publication status: published

Source: online PHE report

Author COI: none 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Peto 2021(d) *(Continued)*
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

PHE 2020
Study characteristics

Patient Sampling	<p>Set of studies conducted by PHE and University of Oxford. This extraction relates to a single-group study estimating sensitivity and specificity: samples obtained during a COVID-19 outbreak at a Navy barracks (n = 157 samples reported in preprint; 2x2 data provided by study investigators)</p> <p>See other 2021 studies by Peto and colleagues for other PHE substudies of Innova assay</p> <p>Recruitment: unclear; presume consecutive</p> <p>Prospective or retrospective: retrospective</p>
Patient characteristics and setting	<p>Setting: outbreak investigation</p> <p>Location: not stated</p> <p>Country: UK</p>

PHE 2020 (Continued)

	<p>Dates: not stated</p> <p>Symptoms and severity: not stated</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: Innova SARS-CoV-2 Antigen Rapid Qualitative Test</p> <p>Manufacturer: Innova Medical Group</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: OP swab used; self-collected</p> <p>Transport media: VTM</p> <p>Sample storage: transported at 4 °C to Porton Down for testing</p> <p>Test operator: laboratory staff</p> <p>Definition of test positivity: visual line; as per manufacturer IFU</p> <p>Blinding reported: not stated</p> <p>Timing of samples: 1 week after outbreak; no further details</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; not described. The preprint supplementary materials describes using the "Roche platform" under the Phase 3b heading, and also provides the following text under the Phase 2 evaluation heading "Unless otherwise stated, all RT-PCR testing was undertaken on the Roche Cobas 6800 or 8800 system using their proprietary SARS-CoV-2 assay as per manufacturer IFU (with off-board lysis using AVL buffer (Qiagen) and 5% Triton-X100 (Sigma Aldrich)). This assay detects ORF-1a/b as a SARS-CoV-2 specific target, and the E-gene as a pan-sarbecovirus target."</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): not stated</p> <p>Samples used: appears to be same sample as for Ag test</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same swab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: failure rate reported as 6/157, 3.8% (Table 4 of preprint)NB resulting no. samples per group (n = 151) does not quite match with final number reported (n = 152)</p> <p>Indeterminate results (index test): unclear</p> <p>Indeterminate results (reference standard): unclear</p>

PHE 2020 (Continued)

Unit of analysis: participant

Comparative

Notes

Funding: PHE evaluation

Publication status: published and unpublished

Source: online PHE report, plus additional data provided by evaluation team

Author COI: none 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		

PHE 2020 (Continued)

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

Pickering 2021(a) [A]
Study characteristics

Patient Sampling	<p>Multi group study estimating sensitivity and specificity: all swabs selected from those submitted to the diagnostic laboratory</p> <p>[1] PCR+ve swabs selected to cover a wide range of Ct values (14-39) (n = 100)</p> <p>[2] PCR-ve swabs (n = 100)</p> <p>[1] and [2] used for comparison of 6 RDTs; included as Pickering 2021(a) [A]</p> <p>[3] PCR+ve swabs with culture results for assessment of infectivity (3 RDTs compared) (n = 141); included as Pickering 2021(b) [A]</p> <p>[4] PCR+ve swabs infected from the B.1.1.7 variant (2 RDTs compared) (n = 23); included as Pickering 2021(c) [A]</p> <p>(Routinely collected serum samples also reported for antibody testing but not further considered for this review)</p> <p>Recruitment: unclear; deliberate sampling</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): [1] + [2] 200 (100)</p>
Patient characteristics and setting	<p>Setting: unclear; swabs submitted to the diagnostic laboratory for routine testing</p> <p>Location: Viapath Infection Sciences laboratory, St Thomas' Hospital, London (Department of Infectious Diseases, School of Immunology & Microbial Sciences, King's College London)</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(a) [A] (Continued)

Country: UK

Dates: [1] to [3] March-October 2020
[4] January 2021

Symptoms and severity: not stated

Demographics: not stated

Exposure history: not stated

Index tests

Test name:

[A] Innova
[B] E25 Bio
[C] Sure Screen V (COVID19 AGVCT)
[D] Spring (SP-SW 106)
[E] Encode
[F] Sure Screen F (COVID19 AGC)

Manufacturer:

[A] Innova Med Group, China
[B] E25 Bio, USA
[C] Sure Screen Diagnostics Ltd
[D] Spring Healthcare, UK
[E] Encode/Emmo Pharma
[F] Sure Screen Diagnostics Ltd

Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"

Ag target: not reported

Test method: **[A], [B], [D] CGIA**
[C], [E] LFA (not otherwise specified)
[F] FIA

Samples used: combined nasal/OP

Transport media: VTM (1 mL)

Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis
[50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]

Test operator: not specified; lab-based

Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.
CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).

Blinding reported: unclear

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: PCR; AusDiagnostics Multiplex Tandem SARS-CoV-2 PCR assays used for diagnosis. Additional PCR testing used an in-house PCR. Viral culture performed using Vero.E6 cells; incubated for 48 h

Definition of non-COVID cases: single negative PCR

Pickering 2021(a) [A] (Continued)

Genetic target(s): N gene or human RNase P

Samples used: combined nasal/OP; same as for index

Timing of reference standard: not stated

Blinded to index test: yes, PCR performed before index test

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: "Department of Health via a National Institute for Health Research comprehensive Biomedical Research Centre award to Guy's and St. Thomas' NHS Foundation Trust in partnership with King's College London and King's College Hospital NHS Foundation Trust"

Publication status: preprint

Source: medRxiv

Author COI: authors report 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?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			

Pickering 2021(a) [A] *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(a) [B]
Study characteristics

Patient Sampling	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] Innova [B] E25 Bio [C] Sure Screen V (COVID19 AGVCT) [D] Spring (SP-SW 106) [E] Encode [F] Sure Screen F (COVID19 AGC)</p> <p>Manufacturer:</p> <p>[A] Innova Med Group, China [B] E25 Bio, USA [C] Sure Screen Diagnostics Ltd [D] Spring Healthcare, UK [E] Encode/Emmo Pharma [F] Sure Screen Diagnostics Ltd</p> <p>Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"</p> <p>Ag target: not reported</p> <p>Test method: [A], [B], [D] CGIA [C], [E] LFA (not otherwise specified) [F] FIA</p> <p>Samples used: combined nasal/OP</p> <p>Transport media: VTM (1 mL)</p> <p>Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis [50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]</p> <p>Test operator: not specified; lab-based</p> <p>Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual. CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).</p> <p>Blinding reported: unclear</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(a) [B] *(Continued)*

Comparative

 Notes Comparative study of 6 Ag tests; [Pickering 2021\(a\) \[A\]](#) details the full study characteristics and QUADAS.

Pickering 2021(a) [C]
Study characteristics

 Patient Sampling Comparative study of 6 Ag tests; [Pickering 2021\(a\) \[A\]](#) details the full study characteristics and QUADAS.

 Patient characteristics and setting Comparative study of 6 Ag tests; [Pickering 2021\(a\) \[A\]](#) details the full study characteristics and QUADAS.

Index tests

Test name:

[A] Innova
 [B] E25 Bio
[C] Sure Screen V (COVID19 AGVCT)
 [D] Spring (SP-SW 106)
 [E] Encode
 [F] Sure Screen F (COVID19 AGC)

Manufacturer:

[A] Innova Med Group, China
 [B] E25 Bio, USA
[C] Sure Screen Diagnostics Ltd,
 [D] Spring Healthcare, UK
 [E] Encode/Emmo Pharma
 [F] Sure Screen Diagnostics Ltd

Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"

Ag target: not reported

Test method: [A], [B], [D] CGIA
 [C], [E] LFA (not otherwise specified)
 [F] FIA

Samples used: combined nasal/OP

Transport media: VTM (1 mL)

Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis
 [50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]

Test operator: not specified; lab-based

Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.
 CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).

Blinding reported: unclear

Timing of samples: not stated

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(a) [C] *(Continued)*

Target condition and reference standard(s)	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.

Pickering 2021(a) [D]
Study characteristics

Patient Sampling	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] Innova [B] E25 Bio [C] Sure Screen V (COVID19 AGVCT) [D] Spring (SP-SW 106) [E] Encode [F] Sure Screen F (COVID19 AGC)</p> <p>Manufacturer:</p> <p>[A] Innova Med Group, China [B] E25 Bio, USA [C] Sure Screen Diagnostics Ltd [D] Spring Healthcare, UK [E] Encode/Emmo Pharma [F] Sure Screen Diagnostics Ltd</p> <p>Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"</p> <p>Ag target: not reported</p> <p>Test method: [A], [B], [D] CGIA [C], [E] LFA (not otherwise specified) [F] FIA</p> <p>Samples used: combined nasal/OP</p> <p>Transport media: VTM (1 mL)</p> <p>Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis [50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]</p> <p>Test operator: not specified; lab-based</p> <p>Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(a) [D] *(Continued)*

CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).

Blinding reported: unclear

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.

Pickering 2021(a) [E]
Study characteristics

Patient Sampling	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] Innova [B] E25 Bio [C] Sure Screen V (COVID19 AGVCT) [D] Spring (SP-SW 106) [E] Encode [F] Sure Screen F (COVID19 AGC)</p> <p>Manufacturer:</p> <p>[A] Innova Med Group, China [B] E25 Bio, USA [C] Sure Screen Diagnostics Ltd [D] Spring Healthcare, UK [E] Encode/Emmo Pharma [F] Sure Screen Diagnostics Ltd</p> <p>Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"</p> <p>Ag target: not reported</p> <p>Test method: [A], [B], [D] CGIA [C], [E] LFA (not otherwise specified) [F] FIA</p> <p>Samples used: combined nasal/OP</p> <p>Transport media: VTM (1 mL)</p> <p>Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis</p>

Pickering 2021(a) [E] *(Continued)*

[50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]

Test operator: not specified; lab-based

Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.

CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).

Blinding reported: unclear

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.

Pickering 2021(a) [F]

Study characteristics

Patient Sampling	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] Innova [B] E25 Bio [C] Sure Screen V (COVID19 AGVCT) [D] Spring (SP-SW 106) [E] Encode [F] Sure Screen F (COVID19 AGC)</p> <p>Manufacturer:</p> <p>[A] Innova Med Group, China [B] E25 Bio, USA [C] Sure Screen Diagnostics Ltd [D] Spring Healthcare, UK [E] Encode/Emmo Pharma [F] Sure Screen Diagnostics Ltd</p> <p>Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"</p> <p>Ag target: not reported</p> <p>Test method: [A], [B], [D] CGIA [C], [E] LFA (not otherwise specified) [F] FIA</p>

Pickering 2021(a) [F] *(Continued)*

Samples used: combined nasal/OP

Transport media: VTM (1 mL)

Sample storage: stored at -80°C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis

[50 μL of stored swab was mixed with 100 μL of buffer supplied with the test kit, and 100 μL of this was applied to the test cassette]

Test operator: not specified; lab-based

Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.

CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).

Blinding reported: unclear

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 6 Ag tests; Pickering 2021(a) [A] details the full study characteristics and QUADAS.

Pickering 2021(b) [A]
Study characteristics

Patient Sampling	<p>Multi-group study estimating sensitivity and specificity: all swabs selected from those submitted to the diagnostic laboratory</p> <p>[3] RT-PCR+ve swabs with culture results for assessment of infectivity (3 RDTs compared) (n = 141); included as Pickering 2021(b) [A]</p> <p>A further 3 groups were reported:</p> <p>[1] RT-PCR+ve swabs selected to cover a wide range of Ct values (14-39) (n = 100) and [2] RT-PCR -ve swabs (n = 100) used for comparison of 6 RDTs; included as Pickering 2021(a) [A]</p> <p>[4] RT-PCR+ve swabs infected from the B.1.1.7 variant (2 RDTs compared) (n = 23); included as Pickering 2021(c) [A]</p> <p>(Routinely collected serum samples also reported for antibody testing but not further considered for this review)</p> <p>Recruitment: unclear; deliberate sampling</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): [2] 141 (141)</p>
Patient characteristics and setting	<p>Setting: unclear; swabs submitted to the diagnostic laboratory for routine testing</p> <p>Location: Viapath Infection Sciences laboratory, St Thomas' Hospital, London (Department of Infectious Diseases, School of Immunology & Microbial Sciences, King's College London)</p> <p>Country: UK</p> <p>Dates: [1] to [3] March-October 2020</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(b) [A] (Continued)

[4] January 2021
Symptoms and severity: not stated
Demographics: not stated
Exposure history: not stated

Index tests

Test name:

[A] Innova
[B] Encode
[C] Sure Screen F (COVID19 AGC)

Manufacturer:

[A] Innova Med Group, China
[B] Encode/Emmo Pharma
[C] Sure Screen Diagnostics Ltd

Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"

Ag target: not reported

Test method: [A] CGIA
[B] LFA (not otherwise specified)
[C] FIA

Samples used: combined nasal/OP

Transport media: VTM (1 mL)

Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis
[50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]

Test operator: not specified; lab-based

Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.
CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).

Blinding reported: unclear

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: RT-PCR; AusDiagnostics Multiplex Tandem SARS-CoV-2 PCR assays used for diagnosis.
Additional PCR testing used an in-house RT-PCR
Viral culture performed using Vero.E6 cells; incubated for 48 h

Definition of non-COVID cases:

Genetic target(s): N gene or human RNase P

Samples used: combined nasal/OP; same as for index

Timing of reference standard: not stated

Blinded to index test: yes, PCR performed before index test

Incorporated index test: no

Pickering 2021(b) [A] (Continued)

Flow and timing	Time interval between index and reference tests: same swab All participants received same reference standard: yes Missing data: yes; insufficient sample volume to conduct all 3 tests on all 141 samples; 31 missing for Innova and 51 missing for Encode Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
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Comparative

Notes	Funding: "Department of Health via a National Institute for Health Research comprehensive Biomedical Research Centre award to Guy's and St. Thomas' NHS Foundation Trust in partnership with King's College London and King's College Hospital NHS Foundation Trust" Publication status: preprint Source: medRxiv Author COI: authors report no COI present
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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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		

Pickering 2021(b) [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?

High

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

Low risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

High risk

Pickering 2021(b) [B]
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(b) [B] (Continued)

Patient Sampling	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] Innova [B] Encode [C] Sure Screen F (COVID19 AGC)</p> <p>Manufacturer:</p> <p>[A] Innova Med Group, China [B] Encode/Emmo Pharma [C] Sure Screen Diagnostics Ltd</p> <p>Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"</p> <p>Ag target: not reported</p> <p>Test method: [A] CGIA [B] LFA (not otherwise specified) [C] FIA</p> <p>Samples used: combined nasal/OP</p> <p>Transport media: VTM (1 mL)</p> <p>Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis [50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]</p> <p>Test operator: not specified; lab-based</p> <p>Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual. CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).</p> <p>Blinding reported: unclear</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.

Pickering 2021(b) [C]
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(b) [C] (Continued)

Patient Sampling	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name:</p> <p>[A] Innova [B] Encode [C] Sure Screen F (COVID19 AGC)</p> <p>Manufacturer:</p> <p>[A] Innova Med Group, China [B] Encode/Emmo Pharma [C] Sure Screen Diagnostics Ltd</p> <p>Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"</p> <p>Ag target: not reported</p> <p>Test method: [A] CGIA [B] LFA (not otherwise specified) [C] FIA</p> <p>Samples used: combined nasal/OP</p> <p>Transport media: VTM (1 mL)</p> <p>Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis [50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]</p> <p>Test operator: not specified; lab-based</p> <p>Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual. CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).</p> <p>Blinding reported: unclear</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 Ag tests; Pickering 2021(b) [A] details the full study characteristics and QUADAS.

Pickering 2021(c) [A]
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(c) [A] (Continued)

Patient Sampling

Multi-group study estimating sensitivity and specificity: all swabs selected from those submitted to the diagnostic laboratory

[4] RT-PCR positive swabs infected from the B.1.1.7 variant (2 RDTs compared) (n = 23); included as [Pickering 2021\(c\) \[A\]](#)

A further 3 groups were reported:

[1] RT-PCR positive swabs selected to cover a wide range of Ct values (14-39) (n = 100) and [2] RT-PCR negative swabs (n = 100) used for comparison of 6 RDTs; included as [Pickering 2021\(a\) \[A\]](#)

[3] RT-PCR positive swabs with culture results for assessment of infectivity (3 RDTs compared) (n = 141); included as [Pickering 2021\(b\) \[A\]](#)

(Routinely collected serum samples also reported for antibody testing but not further considered for this review)

Recruitment: unclear; deliberate sampling

Prospective or retrospective: retrospectively

Sample size (cases): [4] 23 (23)

Patient characteristics and setting

Setting: unclear; swabs submitted to the diagnostic laboratory for routine testing

Location: Viapath Infection Sciences laboratory, St Thomas' Hospital, London (Department of Infectious Diseases, School of Immunology & Microbial Sciences, King's College London)

Country: UK

Dates: [4] January 2021

[1] to [3] March-October 2020

Symptoms and severity: not stated

Demographics: not stated

Exposure history: not stated

Index tests

Test name:

[A] Innova

[B] Sure Screen V (COVID19 AGVCT)

Manufacturer:

[A] Innova Med Group, China

[B] Sure Screen Diagnostics Ltd

Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"

Ag target: not reported

Test method: [A] and B]

Samples used: combined nasal/OP

Transport media: VTM (1 mL)

Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis

[50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]

Test operator: not specified; lab-based

Pickering 2021(c) [A] (Continued)

Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.
 CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).

Blinding reported: unclear

Timing of samples: not stated

Target condition and reference standard(s)

Reference standard: RT-PCR; AusDiagnostics Multiplex Tandem SARS-CoV-2 PCR assays used for diagnosis.

Additional PCR testing used an in-house RT-PCR

Viral culture performed using Vero.E6 cells; incubated for 48 h

Definition of non-COVID cases:

Genetic target(s): N gene or human RNase P

Samples used: combined nasal/OP; same as for index

Timing of reference standard: not stated

Blinded to index test: yes, PCR performed before index test

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab

All participants received same reference standard: yes

Missing data: yes; insufficient sample volume to conduct all 3 tests on all 141 samples; 31 missing for Innova and 51 missing for Encode

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: "Department of Health via a National Institute for Health Research comprehensive Biomedical Research Centre award to Guy's and St. Thomas' NHS Foundation Trust in partnership with King's College London and King's College Hospital NHS Foundation Trust"

Publication status: preprint

Source: medRxiv

Author COI: authors report 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

Pickering 2021(c) [A] *(Continued)*

Was a case-control design avoided? No

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pickering 2021(c) [A] *(Continued)*

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Pickering 2021(c) [B]
Study characteristics

Patient Sampling Comparative study of 2 Ag tests; [Pickering 2021\(c\) \[A\]](#) details the full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 2 Ag tests; [Pickering 2021\(c\) \[A\]](#) details the full study characteristics and QUADAS.

Index tests Test name:
 [A] Innova
[B] Sure Screen V (COVID19 AGVCT)
 Manufacturer:
 [A] Innova Med Group, China
[B] Sure Screen Diagnostics Ltd
 Antibody: all nucleocapsid; "Given that the rapid antigen tests rely on antibody detection of SARS-CoV-2 nucleocapsid (N)"
 Ag target: not reported
 Test method: [A] and B
 Samples used: combined nasal/OP
 Transport media: VTM (1 mL)
 Sample storage: stored at -80 °C at the Directorate of Infection, prior to selection and forwarding to KCL laboratories for analysis
 [50 µL of stored swab was mixed with 100 µL of buffer supplied with the test kit, and 100 µL of this was applied to the test cassette]
 Test operator: not specified; lab-based
 Definition of test positivity: visual and according to manufacturer IFU. Results recorded independently by 2 readers and discordant results referred to a third individual.
 CGIA tests scored according to whether the test band was strongly positive (2), clearly positive (1), weakly positive (0.5) or negative (0).
 Blinding reported: unclear

Pickering 2021(c) [B] *(Continued)*

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 2 Ag tests; Pickering 2021(c) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 Ag tests; Pickering 2021(c) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 Ag tests; Pickering 2021(c) [A] details the full study characteristics and QUADAS.

Pilarowski 2020a
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: testing freely available to people of all ages, with or without symptoms. Community workers conducted door-to-door mobilization in 3 census tracts surrounding the testing site 4 days before testing.</p> <p>Recruitment: consecutive (not stated but all who attended were included)</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 3302 (237)</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centres; community testing site</p> <p>Location: plaza at an urban commercial transport hub in the Mission neighbourhood, San Francisco (University of California, San Francisco)</p> <p>Country: USA</p> <p>Dates: 22 November-1 December 2020</p> <p>Symptoms and severity: 30.9% (n = 1020) self-reported possible COVID-19 symptoms; results reported for 341 (10%) symptomatic (≤ 7 d pso) and 2402 (90%) asymptomatic or symptomatic (> 7 d pso)</p> <p>Of 237 PCR+ve, 95 were asymptomatic, 7 were symptomatic (> 7 d pso), and 135 symptomatic (≤ 7 d pso)</p> <p>Demographics: 1750 (53%) male; 99 (3%) aged < 13 years, 110 (3%) aged 13-18 years, and 3093 (94%) aged > 18 years</p> <p>2166 (66%) Latinx, 304 (9%) Asian, 558 (17%) white, 53 (2%) American Indian, and 83 (3%) black</p> <p>Exposure history: not reported; a setting of ongoing community transmission</p>
Index tests	<p>Test name: BinaxNOW</p> <p>Manufacturer: Abbott</p> <p>Antibody: not reported</p> <p>Ag target: none reported</p> <p>Test method: CGIA</p> <p>Samples used: nasal (AN) (collected by laboratory assistants)</p>

Pilarowski 2020a (Continued)

	<p>Transport media: none used</p> <p>Sample storage: none required; immediate on-site testing</p> <p>Test operator: laboratory technicians (certified technician readers)</p> <p>Definition of test positivity: visual; according to manufacturer IFU</p> <p>Blinding reported: yes performed before PCR</p> <p>Timing of samples: symptomatic with positive Ag result: median 3d (IQR 2-5 d) pso (n = 134)</p>
Target condition and reference standard(s)	<p>Reference standard: PCR (single assay, with positives confirmed on 2nd assay); (1) multiplex PCR conducted by RenegadeBio using RenegadeXP technology; (2) positive results confirmed following US CDC methodology (singleplex PCR) Ct not reported; results reported for ≤ 30 Ct, ≤ 35 Ct, and "no Ct cutoff")</p> <p>Definition of non-COVID cases: same as for cases; single negative PCR for absence of disease</p> <p>Genetic target(s): (1) and (2) N-gene</p> <p>Samples used: nasal (AN) in VTM; paired swab (same site as index)</p> <p>Timing of reference standard: same as for index test</p> <p>Blinded to index test: not reported</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired sample; simultaneous</p> <p>All participants received same reference standard: yes; but only PCR+ on first assay had confirmation on 2nd assay</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "funding for this study was provided by the University of California San Francisco, Program for Breakthrough Biomedical Research, which is partially funded by the Sandler Foundation, a private donor, the Chan Zuckerberg Initiative, and the National Institutes of Health [UM1AI069496]".</p> <p>Publication status: published</p> <p>Source: Clinical Infectious Diseases</p> <p>Author COI: COI declared: "Dr. Havlir reports nonfinancial support from Abbott, outside the submitted work; none of the other authors has any potential conflicts"</p>

Methodological quality

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

Pilarowski 2020a *(Continued)*

Was a consecutive or random sample of patients enrolled? Yes

Was a case-control design avoided? Yes

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pilarowski 2020a *(Continued)*

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Pilarowski 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: mainly asymptomatic suspected patients presenting at a walk-up, free testing at a plaza located at an intersection of the Bay Area-wide subway system (BART) and the San Francisco city bus/street-car system (MUNI), Mission District, California</p> <p>Recruitment: not reported; appears to be all presenting for testing during study period</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 878 (26)</p>
Patient characteristics and setting	<p>Setting: community screening/COVID-19 test centre</p> <p>Location: walk-up/free testing at a community plaza, San Francisco</p> <p>Country: USA</p> <p>Dates: September 2020</p> <p>Symptoms and severity: mainly asymptomatic (84% reported no symptoms during the 14 days before testing)</p> <p>Demographics: 54% male; 77% 18-50 years of age; 81% self-identified as Latinx</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: BinaxNOW COVID-19 Ag Card</p> <p>Manufacturer: Abbott Laboratories</p> <p>Antibody: N protein</p> <p>Ag target: not reported</p> <p>Test method: CGIA</p> <p>Samples used: AN (both nares) (Laboratory technician)</p> <p>Transport media: none required</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pilarowski 2021 (Continued)

	<p>Sample storage: none reported</p> <p>Test operator: laboratory technician; on site</p> <p>Definition of test positivity: visual colour band; each assay was read by 2 independent observers, and a site supervisor served as a tiebreaker. Interpretation amended following first 217 samples because of high FP (9/207 PCR-ve); bands were subsequently scored as positive only if they extended across the full width of the strip, irrespective of the intensity of the band</p> <p>Blinding reported: yes; performed before PCR</p> <p>Timing of samples: mainly asymptomatic; timing not systematically reported for symptomatic group</p>
Target condition and reference standard(s)	<p>Reference standard: PCR (no further details, 2 prior studies cited for reference); in-vitro culture</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): not reported</p> <p>Samples used: AN, paired</p> <p>Timing of reference standard: same as for index</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous, paired</p> <p>All participants received same reference standard: yes</p> <p>Missing data: unclear; 871/878 in the analysis</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "this study was supported by the University of California, San Francisco, the Chan Zuckerberg Biohub, the Chan Zuckerberg Initiative, the San Francisco Latino Task Force, the National Institute of Allergy and Infectious Diseases (grants T32 AI060530 to LR and F31AI150007 to SS), and a private donor."</p> <p>Publication status: published</p> <p>Source: Journal of Infectious Diseases</p> <p>Author COI: all authors reported no COI present</p>

Methodological quality

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

Pilarowski 2021 (Continued)

Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pilarowski 2021 (Continued)

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Pollock 2021a
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity: symptomatic and asymptomatic adults and children who attended the drive-through, free community testing site in Massachusetts

Recruitment: consecutive (all who attended)

Prospective or retrospective: prospective

Sample size (cases): 2482 included; 2308 analysed (292)

Patient characteristics and setting Setting: COVID-19 drive-through testing site; screening (appears to be open to all; no specific testing criteria applied)

Location: the Lawrence General Hospital “Stop the Spread” drive-through testing site, which accommodates Massachusetts residents from the surrounding area.

Country: USA

Dates: 26 October–22 December 2020

Symptoms and severity: adults: 406 (29%) symptomatic; 974 (71%) asymptomatic
 Children: 99 (11%) symptomatic; 829 (89%) asymptomatic
 Adults: median 3 (IQR 2-5) pso days
 Children: median 2 (IQR 1-4) pso days

Demographics: adults: 59% symptomatic female; 56% asymptomatic female
 Age: 19-29 years 332, 24%; 30-49 years 581, 42%; 50-69 years 401, 29%, > 70 years 66, 5%
 Children: 62% symptomatic; 52% asymptomatic female
 Age: < 7 years 261, 28%; 7-13 years 381, 41%; 14-18 years 286, 31%

Exposure history: not reported

Index tests Test name: BinaxNOW COVID-19 Ag Card

Manufacturer: Abbott Diagnostics, USA

Antibody: nucleocapsid protein antigen (by knowledge)

Ag target: not stated

Test method: CGIA (by knowledge)

Samples used: AN (collected by trained operators); both nostrils swabbed; swab rotated 5 times in a circular motion around the inside wall of the nostril for a duration of 10-15 s

Pollock 2021a (Continued)

	<p>Transport media: none; swab placed into a specimen collection bag</p> <p>Sample storage: none; testing within 1 h of collection "tests initiated within an hour of collection time at the temperature of 59°F as per manufacturer's recommendation."</p> <p>Test operator: trained operators</p> <p>Definition of test positivity: visual read-out; test lines recorded as "faint", "medium", or "strong" There was no attempt to resolve any discordance between the 2 readers</p> <p>Blinding reported: yes; conducted before PCR</p> <p>Timing of samples: for symptomatic: adults: median 3 (IQR 2-5) days Children: median 2 (IQR 1-4) days</p>
Target condition and reference standard(s)	<p>Reference standard: PCR; extraction and PCR methods followed the EUA protocol for the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Ct cut-off value of 40</p> <p>Definition of non-COVID cases: same as for cases for symptomatic (single -ve PCR); N/A for asymptomatic</p> <p>Genetic target(s): N2 gene</p> <p>Samples used: AN (paired); transported as dry swab then suspended in swab preservation buffer before testing</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swab; simultaneous</p> <p>All participants received same reference standard: yes</p> <p>Missing data: missing data, n = 54; excluded, n = 94 (samples tested at < 59 °F)</p> <p>Uninterpretable results: inconclusive PCR results n = 26; 1 invalid BinaxNOW result (a manufacturing issue whereby plastic covered the test strip, preventing the buffer from making contact with the test strip); presume test was repeated</p> <p>Indeterminate results (index test): none reported; all FP results had faint but detectable test bands</p> <p>Indeterminate results (reference standard): inconclusive PCR results 189 (n = 26)</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: published version: "supported by Cooperative Agreement Number 1U60OE000103, funded by Centers for Disease Control and Prevention through the Association of Public Health Laboratories."</p> <p>Preprint: "funded by the MA Department of Public Health. The community testing site was funded by the Centers for Disease Control and Prevention Building and Enhancing Epidemiology, Laboratory and Health Information Systems Capacity in Massachusetts –Enhancing Detection COVID Supplement (Grant # 6 NU50CK000518-01-08). BinaxNOW kits were supplied as part of the federal allocation to state health departments."</p> <p>Publication status: published</p> <p>Source: Journal of Clinical Microbiology</p>

Pollock 2021a (Continued)

Author COI: authors report no conflict 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			Unclear
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Pollock 2021a (Continued)

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Pollock 2021b
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity: individuals presenting for testing to a high-throughput, drive-through, free community testing site; no specific criteria for testing had to be met

Recruitment: consecutive

Prospective or retrospective: prospective

Sample size (cases): 1498 (234); from 1603 eligible

Patient characteristics and setting Setting: drive-through testing site; screening
 Location: Lawrence General Hospital "Stop the Spread" drive-through testing site (Department of Laboratory Medicine, Boston Children's Hospital, Boston, MA)

Country: USA

Dates: 11-22 January 2021

Symptoms and severity: 1257 (84%) asymptomatic, including

Pollock 2021b (Continued)

1036/1245 (69%) adults; 209 symptomatic

221/253 (15%) children; 32 symptomatic

Demographics: adult: 57% symptomatic female; 53% asymptomatic female

Children: 56% symptomatic female; 53% asymptomatic female

Age group:

< 7 years: 13 (41%) symptomatic, 60 (27%) asymptomatic

7-13 years: 12 (37) symptomatic, 73 (33%) asymptomatic

14-18 years: 7 (22%) symptomatic, 88 (40%) asymptomatic

19-29 years: 58 (28%) symptomatic, 313 (30%) asymptomatic

30-49 years: 102 (49%) symptomatic, 381 (37%) asymptomatic

50-69 years: 42 (20%) symptomatic, 290 (28%) asymptomatic

> 70 years: 7 (3%) symptomatic, 52 (5%) asymptomatic

Exposure history: not stated

Index tests

Test name: CareStart COVID-19 Antigen test

Manufacturer: Access Bio

Antibody: nucleocapsid

Ag target: not stated

Test method: chromatographic immunoassay

Samples used: AN swab (study site personnel)

Both nostrils swabbed with each swab, alternating which swab was collected first (for PCR vs CareStart)

Transport media: none used

Sample storage: tested within 1 h of collection; median interval between sample collection and test initiation was 31 min (range 12–103 min)

Test operator: trained operators (Master's or PhD-level laboratorians); according to the manufacturer IFU

Definition of test positivity: visual; according to the manufacturer IFU

2 operators read the result; first read of each test was the official result used

Blinding reported: yes; performed before PCR test

Timing of samples: 209 symptomatic adults: median 3 days pso (IQR 2-6)

32 symptomatic children: median 3 days pso (IQR 2-4)

Target condition and reference standard(s)

Reference standard: PCR (CRSP SARS-CoV-2 Real-time Reverse Transcriptase-PCR Diagnostic Assay under EUA);
 Ct cut-off value = 40

Definition of non-COVID cases: as for cases (single -ve for symptomatic)

Genetic target(s): N2 gene

Samples used: AN swab; paired

Timing of reference standard: same as for index

Blinded to index test: unclear

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous

Pollock 2021b (Continued)

All participants received same reference standard: yes

Missing data: 105/1603 (6.5%) (invalid or missing PCR results (n = 48) and missing clinical data (n = 57))

Uninterpretable results: 8 discordant results (all faint positive vs negative); 2 readers disagreed on the strength of the positive band (faint vs 219 medium vs strong) in 7 cases

Indeterminate results (index test): none; states "No invalid CareStart test results were observed."

Indeterminate results (reference standard): 48 invalid or missing PCR results

Unit of analysis: participant

Comparative

Notes

Funding: "Department of Public Health, MA; Centers for Disease Control and Prevention Building and Enhancing Epidemiology, Laboratory and Health Information Systems Capacity in Massachusetts – Enhancing Detection COVID Supplement (Grant # 6 NU50CK000518-01-08). CareStart kits were donated by the manufacturer."

Publication status: preprint

Source: medRxiv preprint

Author COI: authors declare 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		

Pollock 2021b (Continued)

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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

Unclear risk

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

Low concern

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

High risk

Porte 2020
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Porte 2020 (Continued)

Patient Sampling	<p>2-group study to estimate sensitivity and specificity for diagnosis of active disease: samples from suspected COVID-19 cases (n = 1453) with deliberate sampling of PCR –positive and negative cases on a 2:1 basis (n = 127)</p> <p>Recruitment: convenience sampling</p> <p>Prospective or retrospective: retrospective</p> <p>Number of samples (samples with confirmed SARS-CoV-2): 127 (82)</p>
Patient characteristics and setting	<p>Setting: outpatients attending ED at private medical centre (hospital)</p> <p>Location: Clínica Alemana, Santiago</p> <p>Country: Chile</p> <p>Dates: 16-21 March 2020</p> <p>Symptoms and severity: cough 94 (74.6%); fever 77 (61.1%) Median duration of symptoms of 2 days (IQR 1–4; range 0-12) Duration of symptoms: day 0-3 91 (72.2%); day 4-7 27 (22.4%); day ≥ 8 8 (6.3%)</p> <p>Demographics: 68 male (53.5%), median age 38 years (IQR 29.5–44; range 1–91)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: diagnostic Kit for 2019-Novel Coronavirus (2019-nCoV) Ag Test (Cat. N° YRLF04401025, lot N° 2002N408)</p> <p>Manufacturer: Bioeasy Biotechnology Co., Shenzhen, China</p> <p>Ag target: SARS-CoV-2 nucleocapsid protein</p> <p>Antibody: not stated</p> <p>Test method: FIA</p> <p>Samples used: remnant OP and NP swabs in 3 mL UTM</p> <p>Transport media: UTM-RT System, Copan Diagnostics, Murrieta, CA, USA</p> <p>Sample storage: stored at 4 °C and tested within 48 h</p> <p>Test operator: laboratory technician</p> <p>Definition of test positivity: not stated; test "automatically delivers a positive or negative qualitative result" Positive or negative defined qualitatively</p> <p>Blinding reported: yes</p> <p>Timing of samples: on presentation Within 48 h of the PCR test but it doesn't say when PCR test was performed (median duration of symptoms reported in D9)</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR (COVID-19 Genesig Real-Time PCR assay (Primer Design Ltd., Chandler's Ford, UK)); Ct ≤ 40 considered positive</p> <p>Definition of non-COVID cases: single RT-PCR–ve</p> <p>Genetic target(s): not stated</p> <p>Samples used: as for index test; same OP and NP swabs used</p> <p>Timing of reference standard: median 2 d pso (IQR 1-4; range 0-12)</p>

Porte 2020 (Continued)

Blinded to index test: yes (index test done within 48 h of PCR test)

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same sample used; within 48 h

All participants received same reference standard: yes

Missing data: none; participant flow diagram reported

Uninterpretable results: not reported

Indeterminate results (index test): not reported

Indeterminate results (reference standard): not reported

Unit of analysis: participant

Comparative

Notes

Funding: no funding received

Publication status: preprint (not peer-reviewed)

Source: SSRN

Author COI: all study authors declare 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?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Porte 2020 (Continued)

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

High

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

Low risk

Porte 2021 [A]
Study characteristics

Patient Sampling

Multi-group study to estimate sensitivity and specificity:
 (1) COVID-19 patients presenting within 5 days of symptom onset (n = 32)
 (2) symptomatic patients with negative PCR (n = 20)
 (3) asymptomatic patients screened prior to surgery (n = 12)
 (27 PCR+ and 19 PCR- samples were used in 2020 study by Weitzel and colleagues (different assays))

Recruitment: not stated; appears to be convenience

Prospective or retrospective: retrospective

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Porte 2021 [A] (Continued)

Patient characteristics and setting	Setting: private clinic (classed as ED) Location: Clínica Alemana, Santiago Country: Chile Dates: not stated Symptoms and severity: not reported; 12 asymptomatic Demographics: total sample median age 39 years (IQR 36.7-57); 33, 52% male Exposure history: not reported
Index tests	Comparative study of 2 Ag tests (no product codes reported); see Porte 2021 [A] for data related to test [A], Porte 2021 [B] tests [B] data. [A] SOFIA SARS Antigen FIA [B] STANDARD F COVID-19 Ag FIA Manufacturer: [A] Quidel Corporation, San Diego, CA, USA [B] SD Biosensor Inc, Gyeonggi-do, Republic of Korea Antibody: NP (both) Ag target: not stated Test method: both FIA Samples used: NOP flocked swabs; obtained by trained personnel Transport media: UTM-RT System, Copan Diagnostics Sample storage: stored at -80 °C following RT-PCR Test operator: laboratory staff Definition of test positivity: as per manufacturer IFU; both using analyzer device Blinding reported: yes; blinded to RT-PCR result Timing of samples: all < 5 days pso; median PCR+: 2 days (IQR 1-3); PCR-: 1 day (IQR 0.75-4)
Target condition and reference standard(s)	Reference standard: RT-PCR; COVID-19 Genesig, Primerdesign Ltd., Chandler's Ford, UK (Ct) values ≤ 40 were considered positive Definition of non-COVID cases: as for cases Genetic target(s): not stated Samples used: NOP; as for index test Timing of reference standard: not stated Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; same sample All participants received same reference standard: yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Porte 2021 [A] (Continued)

Missing data: none reported, no participant flow diagram reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

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

Source: International Journal of Infectious Disease

Author COI: all authors declare 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?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			

Porte 2021 [A] *(Continued)*
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Porte 2021 [B]
Study characteristics

Patient Sampling	Comparative study of 2 Ag tests; Porte 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	
Index tests	Comparative study of 2 Ag tests (no product codes reported); Porte 2021 [B] data relate to test [B], see Porte 2021 [A] for data related to test [A] and QUADAS entries [A] SOFIA SARS Antigen FIA [B] STANDARD F COVID-19 Ag FIA Manufacturer: [A] Quidel Corporation, San Diego, CA, USA [B] SD Biosensor Inc, Gyeonggi-do, Republic of Korea Antibody: NP (both)

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Porte 2021 [B] *(Continued)*

Ag target: not stated

Test method: both FIA

Samples used: NOP flocked swabs; obtained by trained personnel

Transport media: UTM-RT System, Copan Diagnostics

Sample storage: stored at -80 °C following RT-PCR

Test operator: laboratory staff

Definition of test positivity: as per manufacturer IFU; both using analyzer device

Blinding reported: yes; blinded to RT-PCR result

Timing of samples: all < 5 days pso; median
 PCR+: 2 days (IQR 1-3); PCR-: 1 day (IQR 0.75-4)

Target condition and reference standard(s)	Comparative study of 2 Ag tests; Porte 2021 [A] reports full study characteristics and QUADAS.
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Flow and timing	Comparative study of 2 Ag tests; Porte 2021 [A] reports full study characteristics and QUADAS.
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Comparative	
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Notes	
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Pray 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: symptomatic and asymptomatic participants at 2 universities in Wisconsin (students, staff or other) (n = 1105); at university A, all people tested were eligible (n = 1098), at university B, only students who were quarantined after exposure to people with COVID-19 could participate (n = 47)</p> <p>Recruitment: not stated; appears consecutive/all eligible were included</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 1098 (57) Symptomatic 227 (40) Asymptomatic 871 (17) (1105 paired nasal samples taken; 7 inconclusive Ag or RT-PCR results so excluded from analysis)</p>
Patient characteristics and setting	<p>Setting: University COVID-19 test centre/asymptomatic screening On-site testing: 2 Wisconsin university campuses during university-based testing programmes</p> <p>Location: Wisconsin university campuses</p> <p>Country: USA</p> <p>Dates: 28 September–9 October</p> <p>Symptoms and severity: symptomatic 227 (21%) Asymptomatic 871 (79%) (including 53 with ≥ 1 symptoms in previous 14 days)</p>

Pray 2021 (Continued)

Symptoms included: nasal congestion 114 (50.2%), sore throat 97 (42.7%), headache 87 (38.3%), cough 70 (30.8%), fatigue 60 (26.4%), muscle aches 43 (18.9%), shortness of breath 24 (10.6%)

Demographics: male: 453 (41.3%)

Age group 15-24 years: 971 (88.4%); ≥ 25 years: 127 (11.6%)

Non-Hispanic white: 917 (83.5%)

Exposure history: close contact to the COVID-19 cases in past 14 days: 154 (14%)

Quarantined at time of specimen collection: 135 (12.3%)

Time between quarantine initiation to specimen collection, median days (range): 4 (0-28)

Index tests

Test name: Sofia SARS Antigen Fluorescent Immunoassay (FIA)

Manufacturer: Quidel Corporation

Antibody: not stated

Ag target: not stated

Test method: FIA

Samples used: MTN swab collected by HCWs at university A and were self-collected under supervision at university B

Transport media: none; analysed according to the manufacturer IFU

Sample storage: none; immediate on-site testing

Test operator: presume same HCWs at university A; not reported for university B

Definition of test positivity: not stated; as per manufacturer IFU

Blinding reported: yes- Ag tests were performed before RT-PCR

Timing of samples: median 3d pso (IQR 1, 6 days; 7.5% missing)

152 (72.4%) reported ≤ 5 days from symptom onset to specimen collection

Target condition and reference standard(s)

Reference standard: real-time RT-PCR -

University A: CDC 2019-nCoV assay

University B: TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific)

(Viral culture was attempted on residual RT-PCR specimens if the RT-PCR or Ag test result was positive.)

Definition of non-COVID cases:

Genetic target(s): N1 and N2 viral nucleocapsid protein gene regions

Samples used: nasal swabs stored in viral transport media at 39°F (4 °C)

Timing of reference standard: analysed within 24–72 h of collection.

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous (paired swabs)

All participants received same reference standard: yes; 2 RT-PCR assays used.

Missing data:

7/1105 inconclusive Ag or RT-PCR results excluded from analysis; no details provided

Uninterpretable results: reasons for test 'failure' not reported

Indeterminate results (index test): none reported

Pray 2021 (Continued)

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: not stated

Publication status: published

Source: MMWR US Department of Health and Human Services/Centers for Disease Control and Prevention

Author COI: authors report no COI present

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Yes		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate inclusions?	Yes		
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Could the selection of patients have introduced bias?		Unclear risk	
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Are there concerns that the included patients and setting do not match the review question?			Low concern
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DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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If a threshold was used, was it pre-specified?	Yes		
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Could the conduct or interpretation of the index test have introduced bias?		Low risk	
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Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
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DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Pray 2021 (Continued)

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	High risk

Prince-Guerra 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: any participants who attended 2 sites of Pima County Health Department community-based SARS-CoV-2 testing sites; open to anyone who wanted testing asymptomatic (76%)</p> <p>Recruitment: consecutive; any who attended</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 3419 (299)</p>
Patient characteristics and setting	<p>Setting: community COVID testing sites</p> <p>Location: Pima County, Arizona (Pima County Health Department)</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Prince-Guerra 2021 (Continued)

Country: USA

Dates: 3-17 November 2020

Symptoms and severity: 827 (24%) symptomatic at the time of testing (≥ 1 COVID symptom); 2592 (76%) were asymptomatic

Demographics: median age 41 years (range 10-95); 236 (7%) aged 10–17 years, 1885 (55%) aged 18–49 years, 743 (22%) aged 50–64 years, and 555 (16%) aged ≥ 65 years
1681 (49%) female; 2567 (75%) white; 1075 (31%) Hispanic/Latino

Exposure history: 1138 (33%) had exposure to a diagnosed COVID-19 case (close contact (within 6 ft for ≥ 15 min) in the 14 d before the day of testing with a person with diagnosed COVID-19)

Median days since last exposure 5 (range 0-14)

Index tests

Test name: BinaxNOW COVID-19 Ag Card (BinaxNOW)

Manufacturer: Abbott Diagnostics, USA

Antibody: nucleocapsid

Ag target: not stated

Test method: CGIA

Samples used: AN, bilateral (HCWs)

Transport media: none required

Sample storage: none; immediately tested on-site

Test operator: HCWs

Definition of test positivity: not stated; visual

Blinding reported: yes (performed before PCR)

Timing of samples: day 0-14

Symptomatic: median pso 4 d (range 0-210); 662 (19%) ≤ 7 days; 161 (5%) > 7 days

Target condition and reference standard(s)

Reference standard: RT-PCR; CDC

2019-nCoV Real-Time RT-PCR Diagnostic Panel for detection of SARS-CoV-2 (2,582 swabs) or the Fosun COVID-19 RT-PCR Detection Kit (837 swabs)

Viral culture was performed on 274 of 303 residual real-time RT-PCR specimens with positive results by either test

Definition of non-COVID cases: same as for cases (single -ve PCR)

Genetic target(s): not stated

Samples used: NP, bilateral; obtained after AN swabs (HCW)

Timing of reference standard: as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired swab, simultaneous

All participants received same reference standard: yes

Missing data: none reported

Prince-Guerra 2021 (Continued)

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: Arizona Department of Health Services

Publication status: published

Source: MMWR

Author COI: authors report 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			

Prince-Guerra 2021 (Continued)

Is the reference standards likely to correctly classify the target condition?	Unclear
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Ristic 2021
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: symptomatic patients with ≥ 1 COVID-related symptoms presenting via a triage ambulance of a primary and tertiary out-patients healthcare facility, including a primary care "COVID ambulance" and a "red zone" ambulance</p> <p>Recruitment: consecutive; "all cases"</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 120 (43)</p>
Patient characteristics and setting	<p>Setting: mixed; primary and tertiary outpatients</p> <p>Location: Health Centre Novi Sad and Clinical Centre of Vojvodina, Department for Infectious Diseases</p> <p>Country: Serbia</p> <p>Dates: 21 August-1 September 2020</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Ristic 2021 (Continued)

Symptoms and severity: all symptomatic (120); 103 (86%) with fever, followed by malaise (77, 64%), cough (56, 47%), sore throat (53, 44%), myalgia (46, 38%)

Demographics: median age 49 years (IQR 36–70) (R 14–91 years), female (57) male (63)

Exposure history: not reported

Index tests

Test name: STANDARD Q COVID-19 Ag Test

Manufacturer: SD Biosensor, Gyeonggi-do, South Korea

Antibody: not stated

Ag target: mouse monoclonal anti-SARS CoV-2 antibody (coated in the test line region) and the mouse monoclonal anti-chicken IgY antibody (coated in the control line region)

Test method: chromatographic immunoassay

Samples used: posterior NP by trained medical staff

Transport media: none used for Ag test

Sample storage: no storage

Test operator: trained medical staff

Definition of test positivity: visual interpretation; double lines

Blinding reported: yes; conducted first

Timing of samples: median time from symptom to swab (9.4 days, range 1–45 days; 63 (53%) within first 5 days)

Target condition and reference standard(s)

Reference standard: RT-PCR; a number of assays were described as used - qualitative assessment using 1) AND 2) for each sample and for positive samples only, quantitative assessment of viral load using 3):

1) Argene, SARS-COV-2 R-GENE assay (bioMerieux, Marcy-l'Etoile, France), after RNA extraction

2) Applied Biosystems 7500 Real-Time PCR System (Life Technologies, Carlsbad, CA, USA)

3) COVID-19 Genesig Real-Time PCR Kit (Primerdesign Ltd, Chandler's Ford, UK); Ct < 41 considered positive

Definition of non-COVID cases: single negative

Genetic target(s):

1) R-gene

2) RdRP in the ORF1ab region, E gene, and N gene

3) RdRP

Samples used: unclear (seems to be paired swabs); transported in VTM to a central laboratory and tested within 12 h of collection

Timing of reference standard: same as index

Blinded to index test: unclear

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same time

All participants received same reference standard: yes

Missing data: not stated

Ristic 2021 (Continued)

Uninterpretable results: not stated

Indeterminate results (index test): not stated

Indeterminate results (reference standard): not stated

Unit of analysis: participant

Comparative

Notes

Funding: "supported by Provincial Secretariat for Higher Education and Scientific Research grant"

Publication status: published paper

Source: academic journal

Author COI: no COI statement provided

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			

Ristic 2021 (Continued)

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Rottenstreich 2021
Study characteristics

Patient Sampling	Single-group study estimating sensitivity and specificity: asymptomatic women admitted for delivery Recruitment: consecutive; "all women" Prospective or retrospective: prospective Sample size (cases): 1326 (9)
Patient characteristics and setting	Setting: hospital inpatient Location: Department of Clinical Microbiology and Infectious Diseases Hadassah-Hebrew University Medical Center

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Rottenstreich 2021 (Continued)

Country: Israel
 Dates: 21 October-28 December 2020
 Symptoms and severity: asymptomatic
 Demographics: none stated; all female
 Exposure history: not reported

Index tests

Test name: NowCheck COVID-19 Ag Test
 Manufacturer: Bionote Inc, Hwaseong-si, Republic of Korea
 Antibody: not reported
 Ag target: not reported
 Test method: not reported
 Samples used: NP
 Transport media: not reported
 Sample storage: not reported
 Test operator: not reported
 Definition of test positivity: not reported
 Blinding reported: not reported
 Timing of samples: on admission

Target condition and reference standard(s)

Reference standard: PCR
 (NeuMoDx 288 Molecular System (NeuMoDx Molecular, Ann Arbor, MI)
 Definition of non-COVID cases: single negative
 Genetic target(s): not reported
 Samples used: not reported; states women were "co-tested" so may have been paired swabs
 Timing of reference standard: same as index
 Blinded to index test: not reported
 Incorporated index test: no

Flow and timing

Time interval between index and reference tests: unclear appears to be same time
 All participants received same reference standard: yes
 Missing data: none reported
 Uninterpretable results: none reported
 Indeterminate results (index test): none reported
 Indeterminate results (reference standard): none reported
 Unit of analysis: participant

Rottenstreich 2021 (Continued)

Comparative

Notes

Funding: no funding statement provided

Publication status: published research letter

Source: academic journal

Author COI: no COI statement provided

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Rottenstreich 2021 (Continued)

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

Low concern

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Saeed 2021 [A]
Study characteristics

Patient Sampling

Single-group study to estimate sensitivity alone: RT-PCR+ve samples from suspected cases of COVID-19 (respiratory symptom and/or fever and international travel history or close contact with COVID-19-confirmed patients); it is not clear but seems that both NP and saliva had to be RT-PCR+ve

Recruitment: unclear; states samples were "pre-selected" from a population of 33,000 suspected cases but does not state how many were RT-PCR+ve

Prospective or retrospective: retrospective

Sample size (cases): 100 (100)

Patient characteristics and setting

Setting: COVID-19 diagnostic centre

Location: Islamabad Diagnostic Center (IDC G8 branch specialized centre for COVID-19), Islamabad, (Department of Research and Development, Islamabad Diagnostic Center, F8 Markaz, Islamabad 44000, Pakistan)

Country: Pakistan

Dates: 3-10 October 2020

Symptoms and severity: all symptomatic (respiratory symptoms and/or fever)

Demographics: mean age 47 years (range 6–91); 34 (34%) female; 4 (4%) children

Exposure history: all either had international travel history or close contact with COVID-19 confirmed patients

Index tests

Test name: **[A] NP-based RDT (#20CG2701X)**
 [B] saliva-based RDT (#901101)

Manufacturer: [A] and [B] Lepu Medical, China

Antibody: N gene

Ag target: monoclonal antibody

Saeed 2021 [A] (Continued)

	<p>Test method: CGIA</p> <p>Samples used: [A] NP and [B] saliva; (states collection by trained personnel; saliva would be self-collected)</p> <p>Transport media: not stated</p> <p>Sample storage: not stated</p> <p>Test operator: not stated</p> <p>Definition of test positivity: visual colour lines; performed according to standard manufacturer protocol</p> <p>Blinding reported: unclear</p> <p>Timing of samples: no details</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Bio-rad, CFX96, USA used to identify confirmed PCR+ve cases for RDT testing (exponential growth curve and Ct ≤ 40 considered positive); samples re-tested using #RP10244 years Allplex 2019-nCoV Assay (Seegene South Korea) presumably to quantify viral load</p> <p>Discrepant results were re-tested</p> <p>Definition of non-COVID cases: same as for cases (single -ve PCR)</p> <p>Genetic target(s): Biorad: E gene, N gene, and RNA polymerase gene</p> <p>Samples used: appears that both NP and saliva samples underwent RT-PCR and both were positive. States, "The same patient saliva samples (RT-PCR tested positive)"</p> <p>Timing of reference standard: no details</p> <p>Blinded to index test: yes (performed before index test)</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: discussion states same swabs used</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported; the samples with discordant results were repeated but no details given</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: none</p> <p>Publication status: published</p> <p>Source: Virology Journal</p> <p>Author COI: authors reported no COI present</p>

Methodological quality

Saeed 2021 [A] (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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High

Saeed 2021 [A] (Continued)

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Saeed 2021 [B]
Study characteristics

Patient Sampling	Comparative study of 2 sample types; Saeed 2021 [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	
Index tests	Test name: [A] NP-based RDT (#20CG2701X) [B] saliva-based RDT (#901101) Manufacturer: [A] and [B] Lepu Medical, China Antibody: N gene Ag target: monoclonal antibody Test method: CGIA Samples used: [A] NP and [B] Saliva ; (states collection by trained personnel; saliva would be self-collected) Transport media: not stated Sample storage: not stated Test operator: not stated Definition of test positivity: visual colour lines; performed according to standard manufacturer protocol Blinding reported: unclear Timing of samples: no details
Target condition and reference standard(s)	Comparative study of 2 sample types; Saeed 2021 [A] reports full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 sample types; Saeed 2021 [A] reports full study characteristics and QUADAS.

Saeed 2021 [B] (Continued)

Comparative

Notes Comparative study of 2 sample types; [Saeed 2021 \[A\]](#) reports full study characteristics and QUADAS.

Salvagno 2021

Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: consecutive patients referred to a hospital for SARS-CoV-2 diagnostic testing</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: unclear; "investigation was based on pre-existing specimens, already collected for routine SARS-CoV-2 diagnostic testing in the local facility"</p> <p>Sample size (cases): 321 (149)</p>
Patient characteristics and setting	<p>Setting: unclear; possibly inpatient</p> <p>Location: Pederzoli Hospital, Peschiera del Garda, Verona</p> <p>Country: Italy</p> <p>Dates: 16–30 November 2020</p> <p>Symptoms and severity: not reported; presume symptomatic (patients were, "referred for SARS-CoV-2 diagnostic testing to the Pederzoli Hospital")</p> <p>Demographics: mean age 46 years (IQR 32-56 years); 181 (56%) women</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: SARS-CoV-2 Rapid Antigen Test</p> <p>Manufacturer: Roche</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: NP (reported in Abstract); collection not described</p> <p>Transport media: virus swab UTM, Copan, Brescia, Italy</p> <p>Sample storage: not stated</p> <p>Test operator: not stated</p> <p>Definition of test positivity: visual line</p> <p>Blinding reported: unclear</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Seegene Allplex™2019-nCoV Assay, Seegene, Seoul, South Korea</p>

Salvagno 2021 (Continued)

Threshold: Ct < 37 for all 3 SARS-CoV-2 gene targets considered “reactive” for SARS-CoV-2 RNA

Definition of non-COVID cases: single negative

Genetic target(s): N, E and RdRP

Samples used: same as for index; same swab

Timing of reference standard: not stated

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same swab

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: no research funding declared

Publication status: published

Source: Diagnosis

Author COI: authors state 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		

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Salvagno 2021 (Continued)

If a threshold was used, was it pre-specified?	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?		High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Schildgen 2021 [A]
Study characteristics

Patient Sampling	Unclear design; appears to be single cohort with deliberate sampling of PCR+ve/PCR-: [1] RT-PCR+ve, positive BAL or throat wash samples (n = 42) [2] RT-PCR-ve samples (n = 31) Described as pilot sample panel Recruitment: appears to be convenience
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Schildgen 2021 [A] (Continued)

	Prospective or retrospective: not stated; presume retrospective
Patient characteristics and setting	Setting: not stated Location: authors' institution: Kliniken der Stadt Köln gGmbH (Köln city clinics) Country: Germany Dates: not stated Symptoms and severity: not stated for BAL samples, throat wash from 23 symptomatic and 27 asymptomatic people Demographics: not stated Exposure history: not stated
Index tests	Comparative study of 3 Ag tests (no product codes reported); Schildgen 2021 [A] data relate to test [A], see Schildgen 2021 [B] and Schildgen 2021 [C] for data related to tests [B] and [C]. Test name: [A] BIOCREDIT [B] Panbio [C] SARS-CoV-2 Rapid Antigen test Manufacturer: [A] RapiGEN [B] Abbott [C] Roche Antibody: not stated Ag target: not stated Test method: all LFA Samples used: BAL (n = 13); throat wash (n = 50, including 27 from asymptomatic) Transport media: not stated Sample storage: not stated Test operator: not stated; presume lab staff Definition of test positivity: as per manufacturer IFU Blinding reported: not stated Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR; RealStar SARS-CoV-2 RT-PCR Kit, Altona, Germany Definition of non-COVID cases: as for cases Genetic target(s): not stated Samples used: BAL or throat wash; as per index test Timing of reference standard: not stated Blinded to index test: not stated

Schildgen 2021 [A] (Continued)

	Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same swab All participants received same reference standard: yes Missing data: 8 PCR invalid samples also tested; 2/8 invalid in 1 Ag assay each, 3/8 negative in all 3 Ag assays Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: unclear
Comparative	
Notes	Funding: the study did not receive any external funding Publication status: preprint Source: medRxiv Author COI: the authors declare that they have 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?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	

Schildgen 2021 [A] (Continued)

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Schildgen 2021 [B]
Study characteristics

Patient Sampling Comparative study of 3 Ag tests; [Schildgen 2021 \[A\]](#) reports full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 3 Ag tests; [Schildgen 2021 \[A\]](#) reports full study characteristics and QUADAS.

Index tests Comparative study of 3 Ag tests (no product codes reported); [Schildgen 2021 \[B\]](#) data relate to test [B], see [Schildgen 2021 \[A\]](#) and [Schildgen 2021 \[C\]](#) for data related to tests [A] and [C], and for QUADAS entries.

Test name:

[A] BIOCREDIT
 [B] Panbio

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Schildgen 2021 [B] *(Continued)*

[C] SARS-CoV-2 Rapid Antigen test

Manufacturer:

[A] RapiGEN

[B] Abbott

[C] Roche

Antibody: not stated

Ag target: not stated

Test method: all LFA

Samples used: BAL (n = 13); throat wash (n = 50, including 27 from asymptomatic)

Transport media: not stated

Sample storage: not stated

Test operator: not stated; presume lab staff

Definition of test positivity: as per manufacturer IFU

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 3 Ag tests; Schildgen 2021 [A] reports full study characteristics and QUADAS.
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Flow and timing	Comparative study of 3 Ag tests; Schildgen 2021 [A] reports full study characteristics and QUADAS
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Comparative	
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Notes	
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Schildgen 2021 [C]
Study characteristics

Patient Sampling	Comparative study of 3 Ag tests; Schildgen 2021 [A] reports full study characteristics and QUADAS
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Patient characteristics and setting	Comparative study of 3 Ag tests; Schildgen 2021 [A] reports full study characteristics and QUADAS.
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Index tests	Comparative study of 3 Ag tests (no product codes reported); Schildgen 2021 [C] data relate to test [C], see Schildgen 2021 [A] and Schildgen 2021 [B] for data related to tests [A] and [B], and for QUADAS entries.
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Test name:

[A] BIOCREDIT

[B] Panbio

[C] SARS-CoV-2 Rapid Antigen test

Manufacturer:

[A] RapiGEN

[B] Abbott

[C] Roche

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Schildgen 2021 [C] *(Continued)*

Antibody: not stated

Ag target: not stated

Test method: all LFA

Samples used: BAL (n = 13); throat wash (n = 50, including 27 from asymptomatic)

Transport media: not stated

Sample storage: not stated

Test operator: not stated; presume lab staff

Definition of test positivity: as per manufacturer IFU

Blinding reported: not stated

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 3 Ag tests; Schildgen 2021 [A] reports full study characteristics and QUADAS.
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Flow and timing	Comparative study of 3 Ag tests; Schildgen 2021 [A] reports full study characteristics and QUADAS.
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Comparative	
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Notes	
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Schuit 2021(a)
Study characteristics

Patient Sampling	<p>Report of 2 single-group studies estimating sensitivity and specificity: (1) West Brabant testing sites used the BD Veritor system (included as Schuit 2021(a)) and (2) Rotterdam sites used SD Biosensor assay (included as Schuit 2021(b)).</p> <p>Included close contacts (aged ≥ 16 years) of confirmed COVID-19 cases presenting at testing sites for a 5th-day test (as recommended by Dutch public health service test-and-trace programme, and/or the Dutch contact tracing mobile phone application (the 'CoronaMelder' app) and/or an individual with a confirmed SARS-CoV-2 infection); all asymptomatic at the time of the test request.</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 2692 (233) 2692/3237 agreed to participate</p>
Patient characteristics and setting	<p>Setting: COVID-19 testing centres</p> <p>Location: West Brabant COVID-19 testing sites (Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht)</p> <p>Country: Netherlands</p> <p>Dates: 14 December 2020-6 February 2021</p>

Schuit 2021(a) (Continued)

	<p>Symptoms and severity: all asymptomatic on test booking; 219, 8.6% reported being symptomatic 0-3 days before test</p> <p>Symptoms included: common cold 167/219, 76%; cough 60, 27%; shortness of breath 25, 11%; fever 13, 6%; loss of taste or smell 6, 3%, muscle ache 18, 8%, other 16, 7%</p> <p>Demographics: mean age 45.9 years (SD 17.6 years); 1304, 48.7% male</p> <p>Exposure history: all exposed to confirmed case</p>
Index tests	<p>Test name: BD Veritor System for Rapid Detection of SARS-CoV-2 Ag-RDT</p> <p>Manufacturer: BD Veritor, Franklin Lakes, NJ, USA</p> <p>Antibody: not reported</p> <p>Ag target: nucleocapsid</p> <p>Test method: unknown; CGIA</p> <p>Samples used: nasal + OP; collected by trained personnel, nasal swab 2.5 cm deep</p> <p>Transport media: none; placed in a sterile dry tube</p> <p>Sample storage: frozen at -20 °C within 30 min of collection; transported to Microvida location Amphia laboratory. Thawed and tested within 6 h of collection</p> <p>Test operator: trained laboratory technician; result confirmed by a second person</p> <p>Definition of test positivity: visual interpretation; Analyser was not used</p> <p>Blinding reported: yes; done first</p> <p>Timing of samples: median 5 days (IQR 5-5) between contact and sampling, range 0-13 days Symptomatic (n = 219), symptoms developed on day of test 17 (7.8%), 1 day prior 64 (29.2%), 2 days prior 51 (23.3%), 3 days prior 83 (37.9%)</p>
Target condition and reference standard(s)	<p>Reference standard: (1) PCR; Cobas SARS-CoV- 2 test on the Cobas 8800 platform (Roche Diagnostics International, Rotkreuz, Switzerland)</p> <p>(2) Used routine national testing data to determine whether any PCR-ve had a subsequent +ve PCR or Ag-RDT result within 10 days</p> <p>Definition of non-COVID cases: single negative for absence</p> <p>Genetic target(s): E, RdRp</p> <p>Samples used: combined nasal+OP in UTM (HiViralTM)</p> <p>Timing of reference standard: same as for index test</p> <p>Blinded to index test: yes; stated to be blinded</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes; 14 excluded</p> <p>Uninterpretable results: 10 with no PCR (n = 3) or PCR invalid (n = 7); all Ag-ve</p> <p>Indeterminate results (index test): 3 inconclusive; all PCR-ve 1 further result excluded but reason not clear from flow diagram</p> <p>Indeterminate results (reference standard): none reported</p>

Schuit 2021(a) (Continued)

Unit of analysis: participant

Comparative

Notes

Funding: funded by the Dutch Ministry of Health, Welfare and Sport

Publication status: preprint

Source: medRxiv

Author COI: none to be disclosed

Methodological quality

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

Was a consecutive or random sample of patients enrolled?	Yes		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate inclusions?	Yes		
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Could the selection of patients have introduced bias?		Low risk	
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Are there concerns that the included patients and setting do not match the review question?			Low concern
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DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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If a threshold was used, was it pre-specified?	Yes		
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Could the conduct or interpretation of the index test have introduced bias?		Low risk	
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Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
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DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Schuit 2021(a) *(Continued)*

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

Schuit 2021(b)
Study characteristics

Patient Sampling	<p>Report of 2 single-group studies estimating sensitivity and specificity: (1) West Brabant testing sites used the BD Veritor system (included as Schuit 2021(a)) and (2) Rotterdam sites used SD Biosensor assay (included as Schuit 2021(b)).</p> <p>Included close contacts (aged ≥ 16 years) of confirmed COVID-19 cases presenting at testing sites for a 5th-day test (as recommended by Dutch public health service test-and-trace programme, and/or the Dutch contact tracing mobile phone application (the 'CoronaMelder' app) and/or an individual with a confirmed SARS-CoV-2 infection); all asymptomatic at the time of the test request.</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p>
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Schuit 2021(b) (Continued)

Sample size (cases): 1603 (132)
1603/1903 agreed to participate

Patient characteristics and setting

Setting: COVID-19 testing centres

Location: Rotterdam COVID-19 testing sites (Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht)

Country: Netherlands

Dates: 14 December 2020-6 February 2021

Symptoms and severity: all asymptomatic on test booking; 158, 10.1% symptomatic 0-3 days before test

Symptoms included: common cold 123, 78%; cough 24, 15.2%; shortness of breath 12, 8%; fever 9, 6%; loss of taste or smell 5, 3%, muscle ache 5, 3%, other 15, 9.5%

Demographics: mean age 40.7 years (SD 16.4 years); 845, 52.7% male

Exposure history: all exposed to confirmed case

Index tests

Test name: SARS-CoV-2 Rapid Antigen Test

Manufacturer: Roche/SD Biosensor, Basel, Switzerland

Antibody: not reported

Ag target: nucleocapsid

Test method: CGIA

Samples used: NP alone; collected by trained personnel, > 5 cm deep

Transport media: none

Sample storage: conducted immediately on site

Test operator: not stated; performed independently by 2 people

Definition of test positivity: visual interpretation

Blinding reported: yes; done first

Timing of samples: median 5 days (IQR 5-5) between contact and sampling, range 0-11 days

Symptomatic (n = 158), symptoms developed on day of test 14 (8.9%), 1 day prior 37 (23.4%), 2 days prior 39 (24.7%), 3 days prior 45 (28.5%)

Target condition and reference standard(s)

Reference standard: (1) RT-PCR; Cobas SARS-CoV- 2 test on the Cobas 8800 platform (Roche Diagnostics International, Rotkreuz, Switzerland).

(2) Used routine national testing data to determine whether any RT-PCR-ve had a subsequent +ve RT-PCR or Ag-RDT result within 10 days

Definition of non-COVID cases: single negative for absence

Genetic target(s): E, RdRp

Samples used: combined NP+OP in UTM (HiViralTM); > 5 cm deep

Timing of reference standard: same as for index

Blinded to index test: yes; stated to be blinded

Incorporated index test: no

Schuit 2021(b) (Continued)

Flow and timing

Time interval between index and reference tests: paired

All participants received same reference standard: yes

Missing data: yes; 7 excluded

Uninterpretable results: 4 with no RT-PCR; all Ag -ve

Indeterminate results (index test): 3 inconclusive excluded; all PCR-ve

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: funded by the Dutch Ministry of Health, Welfare and Sport

Publication status: preprint

Source: medRxiv

Author COI: none to be disclosed

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Schuit 2021(b) *(Continued)*

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Low risk

Schwob 2020(a)

Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity of 3 assays (each tested on a separate cohort of individuals, and extracted as 3 entries: Schwob 2020(a) , Schwob 2020(b) and Schwob 2020(c)): adults recruited from 3 outpatient clinics and meeting testing criteria for COVID-19, either: <ul style="list-style-type: none"> • with ≥ 1 major symptom compatible with COVID-19 (cough, fever, sore throat, anosmia, or ageusia), or
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Schwob 2020(a) (Continued)

- with ≥ 1 minor symptom (rhinitis, myalgia, headache, fatigue, nausea, vomiting, diarrhoea, abdominal pain, urticaria, vesicles) and close contact with a confirmed case of COVID-19.

Recruitment: unclear; appears consecutive. RDT brands were rotated after around 30 positive patients until at least 100 positive per test were reached. Numbers per test were [1] 333 (36%) STANDARD Q, [2] 271 (29%) Panbio, and [3] 324(35%) COVID-VIRO.

Prospective or retrospective: prospective

Sample size (cases): overall: 949 (327 positive by NP PCR, 369 positive by saliva PCR). 2x2 data only available for NP PCR
STANDARD Q assay: 333 (112)

Patient characteristics and setting	<p>Setting: outpatient testing clinic</p> <p>Location: Unisante Bugnon; Unisante Flon; Vidy-Med</p> <p>Country: Switzerland</p> <p>Dates: 25 September-4 November 2020</p> <p>Symptoms and severity: whole sample, all symptomatic: 911, 96% with ≥ 1 major symptom (41% fever, 64% cough, 62% sore throat, 32% anosmia/ageusia) and 4% at least 1 minor symptom (rhinitis, myalgia, headache, fatigue, nausea, vomiting, diarrhoea, abdominal pain, urticaria, vesicles)</p> <p>Demographics: median age: 31 (IQR 25-42; range 18-87); male (51%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: STANDARD Q COVID-Ag Test See Schwob 2020(b) and Schwob 2020(c) for data for Panbio COVID-19 Ag Test (Abbott) and COVID-VIRO (AAZ)</p> <p>Manufacturer: SD Biosensor/Roche</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not stated</p> <p>Test method: lateral flow; no further information</p> <p>Samples used: NP (HCW)</p> <p>Transport media: not stated</p> <p>Sample storage: no storage, immediate</p> <p>Test operator: same HCW who collected the swab</p> <p>Definition of test positivity: visual colour change</p> <p>Blinding reported: yes, done first</p> <p>Timing of samples: pso (mean duration of symptoms at the time of swab collection/testing was 2.6 days (SD 2.3, range 0-30))</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; in-house or Cobas 6800</p> <p>Definition of non-COVID cases: single negative</p> <p>Genetic target(s): E gene</p>

Schwob 2020(a) (Continued)

Samples used: NP; HCW collected (saliva sample also collected but Ag results only presented compared to NP swab)

Timing of reference standard: pso (mean duration of symptoms at the time of swab collection/testing was 2.6 days (SD 2.3, range 0-30))

Blinded to index test: unclear

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same time

All participants received same reference standard: yes

Missing data: yes; 21 excluded due to lack of PCR and/or RDT result, no further details

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative
Notes

Funding: "the RDT and saliva PCR were paid for by the cantonal health authorities"

Publication status: preprint

Source: medRxiv

Author COI: authors report 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		

Schwob 2020(a) *(Continued)*

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Schwob 2020(b)
Study characteristics
Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Schwob 2020(b) (Continued)

Patient Sampling

Single-group study to estimate sensitivity and specificity of 3 assays (each tested on a separate cohort of individuals, and extracted as 3 entries: [Schwob 2020\(a\)](#), [Schwob 2020\(b\)](#) and [Schwob 2020\(c\)](#)): adults recruited from 3 outpatient clinics and meeting testing criteria for COVID-19, either:

- with ≥ 1 major symptom compatible with COVID-19 (cough, fever, sore throat, anosmia, or ageusia), or
- with ≥ 1 minor symptom (rhinitis, myalgia, headache, fatigue, nausea, vomiting, diarrhoea, abdominal pain, urticaria, vesicles) and close contact with a confirmed case of COVID-19

Recruitment: unclear; appears consecutive. RDT brands were rotated after around 30 positive patients until at least 100 positive per test were reached; 333 (36%) STANDARD Q, 271 (29%) Panbio and 324(35%) COVID-VIRO.

Prospective or retrospective: prospective

Sample size (cases): 949 (327 positive by NP PCR, 369 positive by saliva PCR). 2x2 data only available for NP PCR
 Panbio assay: 271 (122)

Patient characteristics and setting

Setting: outpatient testing clinic

Location: Unisante Bugnon; Unisante Flon; Vidy-Med

Country: Switzerland

Dates: 25 September-4 November 2020

Symptoms and severity: whole sample, all symptomatic: 911, 96% with ≥ 1 major symptom (41% fever, 64% cough, 62% sore throat, 32% anosmia/ageusia) and 4% at least one minor symptom (rhinitis, myalgia, headache, fatigue, nausea, vomiting, diarrhoea, abdominal pain, urticaria, vesicles)

Demographics: median age: 31 years (IQR 25-42; range 18-87 years); male (51%)

Exposure history: not stated

Index tests

Test name: Panbio COVID-19 Ag Test
 See [Schwob 2020\(a\)](#) and [Schwob 2020\(c\)](#) for data for STANDARD Q (SD Biosensor) and COVID-VIRO (AAZ)

Manufacturer: Abbott

Antibody: nucleocapsid

Ag target: not stated

Test method: lateral flow; no further information

Samples used: NP (HCW)

Transport media: not stated

Sample storage: no storage, immediate

Test operator: HCW

Definition of test positivity: visual colour change

Blinding reported: yes, done first

Timing of samples: pso (mean duration of symptoms at the time of swab collection/testing was 2.6 days (SD 2.3, range 0-30))

Schwob 2020(b) (Continued)

Target condition and reference standard(s)	Reference standard: RT-PCR; in-house or Cobas 6800 Definition of non-COVID cases: single negative Genetic target(s): E gene Samples used: NP; HCW collected (saliva sample also collected but Ag results only presented compared to NP swab) Timing of reference standard: pso (mean duration of symptoms at the time of swab collection/testing was 2.6 days (SD 2.3, range 0-30)) Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same time All participants received same reference standard: yes Missing data: yes; 21 excluded due to lack of PCR and/or RDT result, no further details (There appears to be a typo in Suppl Fig 1, which reports 122 PCR+ve samples tested with Panbio assay; 101 are shown as RDT+ and 17 RDT-. The text reports assay sensitivity as 86.1% (95% CI 78.6, 91.7%), which works out as 105 RDT+, 17 RDT- and the correct CIs) Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "the RDT and saliva PCR were paid for by the cantonal health authorities" Publication status: preprint Source: medRxiv Author COI: none

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 inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	

Schwob 2020(b) (Continued)

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Schwob 2020(b) (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Schwob 2020(c)
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity of 3 assays (each tested on a separate cohort of individuals, and extracted as 3 entries: Schwob 2020(a), Schwob 2020(b) and Schwob 2020(c)): adults recruited from 3 outpatient clinics and meeting testing criteria for COVID-19, either:</p> <ul style="list-style-type: none"> with ≥ 1 major symptom compatible with COVID-19 (cough, fever, sore throat, anosmia, or ageusia), or with ≥ 1 minor symptom (rhinitis, myalgia, headache, fatigue, nausea, vomiting, diarrhoea, abdominal pain, urticaria, vesicles) and close contact with a confirmed case of COVID-19 <p>Recruitment: unclear; appears consecutive. RDT brands were rotated after around 30 positive patients until at least 100 positive per test were reached; 333 (36%) STANDARD Q, 271 (29%) Panbio and 324(35%) COVID-VIRO.</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): overall: 949 (327 positive by NP PCR, 369 positive by saliva PCR). 2x2 data only available for NP PCR COVID-VIRO assay: 324 (138)</p>
Patient characteristics and setting	<p>Setting: outpatient testing clinic</p> <p>Location: Unisante Bugnon; Unisante Flon; Vidy-Med</p> <p>Country: Switzerland</p> <p>Dates: 25 September-4 November 2020</p> <p>Symptoms and severity: whole sample, all symptomatic: 911, 96% with ≥ 1 major symptom (41% fever, 64% cough, 62% sore throat, 32% anosmia/ageusia) and 4% at least one minor symptom (rhinitis, myalgia, headache, fatigue, nausea, vomiting, diarrhoea, abdominal pain, urticaria, vesicles)</p> <p>Demographics: median age: 31 years (IQR 25-42; range 18-87); male (51%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: COVID-VIRO See Schwob 2020(a) and Schwob 2020(b) for data for STANDARD Q (SD Biosensor) and Panbio COVID-19 Ag Test (Abbott)</p> <p>Manufacturer: AAZ-LMB</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not stated</p> <p>Test method: lateral flow; no further information</p>

Schwob 2020(c) (Continued)

	<p>Samples used: NP (HCW)</p> <p>Transport media: not stated</p> <p>Sample storage: no storage, immediate</p> <p>Test operator: HCW</p> <p>Definition of test positivity: visual colour change</p> <p>Blinding reported: yes, done first</p> <p>Timing of samples: pso (mean duration of symptoms at the time of swab collection/testing was 2.6 days (SD 2.3, range 0-30))</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; in-house or Cobas 6800</p> <p>Definition of non-COVID cases: single negative</p> <p>Genetic target(s): E gene</p> <p>Samples used: NP; HCW collected (saliva sample also collected but Ag results only presented compared to NP swab)</p> <p>Timing of reference standard: pso (mean duration of symptoms at the time of swab collection/testing was 2.6 days (SD 2.3, range 0-30))</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same time</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes; 21 excluded due to lack of PCR and/or RDT result, no further details</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "the RDT and saliva PCR were paid for by the cantonal health authorities"</p> <p>Publication status: preprint</p> <p>Source: medRxiv</p> <p>Author COI: none</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Schwob 2020(c) (Continued)

Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Schwob 2020(c) *(Continued)*

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Scohy 2020
Study characteristics

Patient Sampling Single-group study including NP swabs submitted to laboratory at a large tertiary hospital (n = 148)
 Recruitment: random sample
 Prospective or retrospective: not stated

Patient characteristics and setting Setting: unclear; presume microbiology laboratory takes samples from number of sources
 Location: Cliniques Universitaires Saint-Luc Hospital, Brussels
 Country: Belgium
 Dates: 6-21 April 2020
 Symptoms and severity: 86 (58%) symptomatic, 45 (30%) asymptomatic, 17 (11%) symptom status not reported
 Cases only: viral load < 25 Ct 10 (9%), ≥ 25 Ct 96 (91%)
 Demographics: median age 57.5 (0-94 years); 64 (43%) male
 Exposure history: not reported

Index tests Test name: COVID-19 Ag Respi-Strip (product code not reported)
 Manufacturer: Coris Bioconcept
 Antibody: NP
 Ag target: monoclonal antibody
 Test method: CGIA
 Samples used: NP
 Transport media: not stated
 Sample storage: "If the rapid antigen test was not performed immediately, samples were stored at 4 °C until the test"
 Test operator: not stated

Scohy 2020 (Continued)

	Definition of test positivity: visual appearance of T line; also states that "Two versions of the test were evaluated. On the second version, conjugate was coupled on a different way and the control line was optimized." Blinding reported: unclear Timing of samples: not reported
Target condition and reference standard(s)	Reference standard: RT-PCR: genesig Real-Time PCR assay (Primerdesign Ltd, Chandler's Ford, UK); < 40 Ct Definition of non-COVID cases: single PCR negative Genetic target(s): RdRp Samples used: NP; same as for index Timing of reference standard: not stated Blinded to index test: yes Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same sample All participants received same reference standard: yes Missing data: none reported, no participant flow diagram reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: no funding statement reported; COVID-19 Ag Respi-Strip tests provided by Coris BioConcept. Publication status: published Source: Journal of Clinical Virology Author COI: the authors declare 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		

Scohy 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 (Evaluations of single test application)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)	
DOMAIN 3: Reference Standard	
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Shidlovskaya 2021 [A]

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: patients with suspected COVID-19 admitted to the hospital on day 2-10 pso (fever, dry cough, chest pain and discomfort, shortness of breath, loss of smell and taste). All included patients had CT signs of lung damage.</p> <p>Recruitment: unclear</p> <p>Prospective or retrospective: not stated; may be prospective</p> <p>Sample size (cases): 106 (78)</p>
Patient characteristics and setting	<p>Setting: hospital inpatient</p> <p>Location: infectious diseases hospital, Moscow (Department of Virology, Lomonosov Moscow State University, Moscow)</p> <p>Country: Russia</p> <p>Dates: 25 January-8 February 2021</p> <p>Symptoms and severity: 100% symptomatic; symptoms included fever, dry cough, chest pain and discomfort, shortness of breath, loss of smell and taste; all had lung damage on CT</p> <p>Demographics: mean age 67.7 (range 28-95) years; 53 (50%) female</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: [A] SGTI-flex COVID-19 Ag [B] BIOCREDIT COVID-19 Ag</p> <p>Manufacturer: [A] Sugentech Inc., Korea [B] RapiGEN Inc., Korea</p> <p>Antibody: [A] Nucleocapsid [B] SARS-COV2 antigen</p> <p>Ag target: not stated</p> <p>Test method: [A] LFA [B] CGIA</p> <p>Samples used: NP (collected by nurses)</p> <p>Transport media: none required</p> <p>Sample storage: none required; tested directly at the patient bedside</p> <p>Test operator: nurses</p> <p>Definition of test positivity: visual</p> <p>Blinding reported: yes (performed before PCR)</p> <p>Timing of samples: between 2-10 days pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; one-step "SARS-CoV-2 FRT" commercial kit with catalogue number EA-128 (bought from N.F. Gamaleya NRCEM, Moscow, Russia)</p> <p>Cell culture also used in all PCR+ve samples 293T/ACE2</p>

Shidlovskaya 2021 [A] (Continued)

	Definition of non-COVID cases: same as for cases (single -ve PCR) Genetic target(s): NSP1 gene Samples used: NP Timing of reference standard: 2-10 days pso. Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous; paired All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: the Ministry of Health of the Russian Federation Publication status: preprint Source: medRxiv preprint Author COI: authors declare 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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Shidlovskaya 2021 [A] (Continued)

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Shidlovskaya 2021 [B]
Study characteristics

 Patient Sampling Comparative study of 2 Ag tests; [Shidlovskaya 2021 \[A\]](#) details full study characteristics and QUADAS.

 Patient characteristics and setting Comparative study of 2 Ag tests; [Shidlovskaya 2021 \[A\]](#) details full study characteristics and QUADAS.

Index tests Test name: [A] SGTI-flex COVID-19 Ag

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Shidlovskaya 2021 [B] *(Continued)*

[B] BIOCREDIT COVID-19 Ag

Manufacturer: [A] Sugentech Inc., Korea

[B] RapiGEN Inc., Korea

Antibody: [A] Nucleocapsid

[B] SARS-COV2 antigen

Ag target: not stated

Test method: [A] LFA

[B] CGIA

Samples used: NP (collected by nurses)

Transport media: none required

Sample storage: none required; tested directly at the patient bedside

Test operator: nurses

Definition of test positivity: visual

Blinding reported: yes (performed before PCR)

Timing of samples: between 2-10 days from the onset of symptoms

Target condition and reference standard(s)	Comparative study of 2 Ag tests; Shidlovskaya 2021 [A] details full study characteristics and QUADAS.
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Flow and timing	Comparative study of 2 Ag tests; Shidlovskaya 2021 [A] details full study characteristics and QUADAS.
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Comparative

Notes

Shrestha 2020

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: people who were close contacts of confirmed cases identified through contact tracing, residing in quarantine centre (n = 113)</p> <p>Recruitment: convenience</p> <p>Prospective or retrospective: not stated; appears prospective</p>
Patient characteristics and setting	<p>Setting: contact tracing</p> <p>Location: not applicable; author institutions include Shukraraaj Tropical and Infectious Disease Hospital, Kathmandu</p> <p>Country: Nepal</p> <p>Dates: August-September 2020</p> <p>Symptoms and severity: all asymptomatic</p> <p>Demographics: range 13-74; 89, 79% male</p>

Shrestha 2020 (Continued)

	Exposure history: all exposed to confirmed case
Index tests	<p>Test name: BIOCREDIT</p> <p>Manufacturer: RapiGen</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: NP</p> <p>Transport media: none used</p> <p>Sample storage: none reported; other sample from the same individual was processed for the results as instructed by the manufacturing company of Ag kit</p> <p>Test operator: lab technician (trained)</p> <p>Definition of test positivity: visual line; as per manufacturer IFU</p> <p>Blinding reported: unclear; appears to be Yes</p> <p>Timing of samples: day 5 of quarantine</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; not detailed, "followed the standard protocol regulated by WHO, instruction manual of company and as per NHTC training regarding sample collection and transport"</p> <p>Definition of non-COVID cases: as for cases; single negative</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP in 3 mL VTM</p> <p>Timing of reference standard: as for index test</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous, paired samples</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): tests were repeated for samples with indistinct outcomes.</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: patient</p>
Comparative	
Notes	<p>Funding: no funding statement provided</p> <p>Publication status: published</p>

Shrestha 2020 (Continued)

Source: Kathmandu University Medical Journal

Author COI: no COI statement provided

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			

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Shrestha 2020 (Continued)

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Smith 2021
Study characteristics

Patient Sampling	<p>Single-group longitudinal study estimating sensitivity only: newly PCR+ve (within 24 h) students and employees at University of Illinois identified from routine testing (PCR every 2-4 d) and their close contacts (eligible within 5 d of exposure) who also tested positive during study period. Participants were required to collect paired samples on a daily basis (for 14 d for those with positive PCR prior to enrolment or during quarantine period, and for 7 d for those continuing to test negative on PCR after enrolment). Data were reported only for those with positive viral culture on at least 1 PCR+ve sample.</p> <p>Recruitment: unclear; appears to be consecutive inclusion of those meeting above criteria</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 51 PCR+ve (number eligible not reported)</p>
Patient characteristics and setting	<p>Setting: student/staff screening</p> <p>Location: University of Illinois campus</p> <p>Country: USA</p> <p>Dates: not reported</p> <p>Symptoms and severity: all "mild or asymptomatic", numbers not reported</p> <p>Demographics: mean age 33.1 years (SD 12.8 years); 23, 53.5% male; 34, 79.1% white, 4, 9.3% black, 4, 9.3% 'other', 1, 2.3% Asian</p> <p>Exposure history: all PCR+ve</p>
Index tests	<p>Test name: SOFIA</p> <p>Manufacturer: Quidel</p> <p>Ag target: SARS-CoV</p> <p>Test method: FIA</p> <p>Samples used: nasal</p> <p>Transport media: none used</p> <p>Sample storage: samples collected by courier within 1 h of collection using a no-contact pickup protocol; transported with cold packs, and stored at 4 °C overnight based on guidance from the manufacturer. Tested the morning after collection</p>

Smith 2021 (Continued)

Test operator: not stated; presumably laboratory technician

Definition of test positivity: as per manufacturer IFU

Blinding reported: unclear; saliva PCR was within 12 h of sample collection and RDT was morning after

Timing of samples: those with positive PCR prior to enrolment were tested from within 24 h after first positive result to 14 d after; those testing positive during quarantine period were tested for up to 14 d, and those never positive were tested for 7 d.

Target condition and reference standard(s)

Reference standard: RT-PCR and viral culture

- 1) direct saliva to RT-qPCR assay (in-house, following previously published protocol)
- 2) nasal swabs - Abbott Alinity per manufacturer IFU performed at John's Hopkins
- 3) nasal swabs - viral culture VeroTMPRSS2 cells; presence of SARS-CoV-2 was confirmed through RT-qPCR

Definition of non-COVID cases: as for cases; single negative

Genetic target(s): not stated

Samples used: 1) saliva (tested within 12 h of collection); 2 and 3) nasal swabs in VTM (stored at -80 °C after collection and subsequently shipped to Johns Hopkins University for RT-qPCR and viral culture)

Timing of reference standard: as for index test

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneous, paired samples

All participants received same reference standard: yes

Missing data: Eight individuals were removed from the analysis because their nasal virus culture was never positive

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: patient

Comparative

Notes

Funding: "supported by the National Heart, Lung, and Blood Institute at the National Institutes of Health (grant number 3U54HL143541-02S2) through the RADx-Tech program."

Publication status: published

Source: Journal of Infectious Diseases

Author COI: CBB and LW are listed as inventors on a pending patent application for the saliva RT-qPCR test used in this study. All other authors report no potential conflicts.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Smith 2021 (Continued)

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 inclusions? 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 (Evaluations of single test application)
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

If a threshold was used, was it pre-specified? 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 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Unclear

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

Are there concerns that the target condition as defined by the High

Smith 2021 *(Continued)*
reference standard does not match the question?
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Stohr 2021 [A]
Study characteristics

Patient Sampling Randomized study estimating sensitivity and specificity: adults presenting for testing at a community COVID-19 test centre; testing co-ordinated by the Municipal Health Services (MHS). Participants randomized between 2 different Ag tests.

Recruitment: consecutive

Prospective or retrospective: prospective

Sample size (cases): 3215 (377); [A] 1604, [B] 1611

Patient characteristics and setting Setting: COVID-19 test centre

Location: Municipal Health Services in Tilburg, Noord-Brabant

Country: Netherlands

Dates: 23 December 2020-17 January 2021

Symptoms and severity: current symptoms of COVID-19 2226 (69.2%), symptoms in preceding 3 weeks 201 (6.3%), no current or prior symptoms 788 (24.5%). Definition of COVID-19 symptoms was not provided.

Demographics: median age 41 years (IQR 29-54 years); 1409 (43.8%) male

Exposure history: not reported

Index tests Test name: **[A] BD Veritor System for Rapid Detection of SARS-CoV-2**
 [B] SARS-CoV-2 antigen detection test

Manufacturer: **[A] Becton Dickinson, USA**
 [B] Roche

Antibody: nucleocapsid

Ag target: not stated

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Stohr 2021 [A] (Continued)

	<p>Test method: CGIA</p> <p>Samples used: NMT; self-collected</p> <p>Transport media: none used</p> <p>Sample storage: no storage</p> <p>Test operator: self-tested; written and illustrated booklet provided along with QR-code link to a 2-min online video illustrating NMT self-sampling and self-testing</p> <p>Definition of test positivity: visual</p> <p>Blinding reported: yes</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; either (1) Alinity M SARS-CoV-2 Assay (Abbott) or with (2) a LDT using the QIA-symphony Sample Processing and Rotorgene amplification system (Qiagen, Hilden, Germany)</p> <p>Samples collected before 12 January 2021 were frozen at -80°C within 24 h of collection and transported to the Dutch National Institute for Public Health and the Environment (RIVM) for viral culture]</p> <p>Definition of non-COVID cases: single negative</p> <p>Genetic target(s): (1) N-gene and RdRP-gene target (2) E-gene</p> <p>Samples used: NP+OP in GLY; collected by trained member of the Municipal Health Service</p> <p>Timing of reference standard: as for index test. Tested within 4 h of collection</p> <p>Blinded to index test: unclear; could presume Yes given self-testing</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same day (instructed to self-test immediately on arrival at home)</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes;</p> <p>Uninterpretable results: no PCR due to sample loss (n = 11)</p> <p>Indeterminate results (index test): "inconclusive" Ag assay results (n = 48; 9 PCR+ve and 39 PCR-) were excluded by authors for overall sensitivity and specificity; definition of 'inconclusive' was not reported.</p> <p>Inconclusive results were included for determining the Ct value cut-off at which the chance (P) of having a positive viral culture was $P = 0.5$, and were interpreted as not false negative when determining the variables associated with a false negative result</p> <p>Indeterminate results (reference standard): inconclusive results on PCR (n = 3) were excluded by the authors; all Ag test negative</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: funded by the Dutch Ministry of Health, Welfare and Sports (VWS)</p> <p>Publication status: preprint</p> <p>Source: medRxiv</p>

Stohr 2021 [A] (Continued)

Author COI: none 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

Stohr 2021 [A] *(Continued)*

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias?

High risk

Stohr 2021 [B]
Study characteristics

Patient Sampling Comparative study of 2 Ag tests; [Stohr 2021 \[A\]](#) details full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 2 Ag tests; [Stohr 2021 \[A\]](#) details full study characteristics and QUADAS.

Index tests Test name: [A] BD Veritor System for Rapid Detection of SARS-CoV-2
[B] SARS-CoV-2 antigen detection test

Manufacturer: [A] Becton Dickinson, USA
[B] Roche

Antibody: nucleocapsid

Ag target: not stated

Test method: CGIA

Samples used: NMT; self-collected

Transport media: none used

Sample storage: no storage

Test operator: self-tested; written and illustrated booklet provided along with QR-code link to a 2-min online video illustrating NMT self-sampling and self-testing

Definition of test positivity: visual

Blinding reported: yes

Timing of samples: not stated

Stohr 2021 [B] *(Continued)*

Target condition and reference standard(s)	Comparative study of 2 Ag tests; Stohr 2021 [A] details full study characteristics and QUADAS.
Flow and timing	Comparative study of 2 Ag tests; Stohr 2021 [A] details full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 2 Ag tests; Stohr 2021 [A] details full study characteristics and QUADAS.

Stokes 2021(a) [A]
Study characteristics

Patient Sampling	<p>Report of 3 studies estimating sensitivity and/or specificity. This entry (Stokes 2021(a) [A]) relates to cohort [1]</p> <p>[1] Sensitivity only: symptomatic participants with a recent positive SARS-CoV-2 RT-PCR were invited to contribute further samples for an RDT evaluation; only those who were still PCR+ve on paired swabs are included</p> <p>A second cohort was included as Stokes 2021(b)</p> <p>[2] Sensitivity and specificity: symptomatic individuals presenting to Alberta Health Services community COVID-19 assessment centres within 7 d pso</p> <p>(A third cohort was excluded because of deliberate inclusion of samples containing various non-SARS-CoV-2 respiratory viruses in addition to samples from asymptomatic individuals at low risk of having COVID-19 (all RT-PCR-ve)).</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): (1) 145 (138); 7 RT-PCR-ve at time of second sampling were excluded by the review team</p>
Patient characteristics and setting	<p>Setting: unclear; likely community setting</p> <p>Location: samples tested positive at Alberta Precision Laboratories and confirmed as cases by Alberta Health Services Public Health</p> <p>Country: Canada</p> <p>Dates: not stated</p> <p>Symptoms and severity: all symptomatic; cough (42.8%), headache (42.1%), myalgias (41.4%), sinus congestion (36.6%), malaise (31.0%), pharyngitis (29.0%), fevers/chills (28.3%), anosmia (24.1%), ageusia (24.1%), rhinorrhoea (20.0%), shortness of breath (5.5%), nausea/vomiting (3.4%), and other (17.9%, included chest pain, diarrhoea, eye soreness, lymphadenopathy, loss of appetite, arthralgia, dizziness, and/or conjunctivitis)</p> <p>Demographics: mean age 39.4 years (median 36.0 years, range 18.5-86.6 years); 42.8% male</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Panbio</p> <p>Manufacturer: Abbott, IL, USA</p> <p>Antibody: nucleocapsid</p>

Stokes 2021(a) [A] (Continued)

Ag target: not stated

Test method: CGIA

Samples used: **[A] NP**, [B] OP, [C], saliva

[A] and [B] collected by trained HCWs, [C] was self-collected using ClassiqSwab
Paired NP swabs collected from separate nostrils; OP swabs collected from both sides of the
oropharynx and the posterior pharyngeal wall under the uvula
[B] and [C] sampling was terminated early due to poor sensitivity compared to NP

Transport media: none used; tested immediately

Sample storage: no storage

Test operator: states tested immediately, so presume same HCW

Definition of test positivity: visual line

Blinding reported: yes (conducted first); but not blinded to COVID-19 status (all previously PCR+ve)

Timing of samples: mean duration of symptoms 6.1 d (median 6.0, range 3.0–10.0 days); 91% were
≤ 7 d pso

Target condition and refer-
ence standard(s)

Reference standard: RT-PCR; either an in-house LDT or the Cobas SARS-CoV-2 test on the Cobas
6800 instrument

Definition of non-COVID cases: single negative PCR apart from discrepant results which (FPs) were
re-extracted and retested in triplicate with the N2 assay from the US CDC 2019-Novel Coronavirus
(2019-nCoV) real-time RT-PCR diagnostic panel

Genetic target(s): LDT - E gene (< 35 Ct); Cobas - not reported (2/2 targets positive, or ≥ 1 targets
were positive in duplicate)

Samples used: [A] NP (YOCON) swab and universal transport media (UTM) (Yocon, Beijing, China)
[B] and [C] OP; ClassiqSwabs for throat in COPAN UTM-RT (COPAN Diagnostics, CA, USA)
Both stored at 4 °C upon arrival at the laboratory and tested within 72 h of collection

Timing of reference standard: as for index

Blinded to index test: not stated; may have known samples were from previously PCR+ve cases

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired

All participants received same reference standard: yes

Missing data: yes

Uninterpretable results: 4, Panbio results were not recorded; 1, unable to be processed by RT-PCR;
1, Panbio reported as negative before 15 min

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: 'funded using internal operating funds of Alberta Precision Laboratories and Alberta
Health Services. Test kits and instruments were paid for by the Public Health Agency of Canada.'

Publication status: published

Stokes 2021(a) [A] (Continued)

Source: European Journal of Clinical Microbiology & Infectious Diseases

Author COI: the authors declare that they have 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?	No		
Did the study avoid inappropriate inclusions?	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?			High
DOMAIN 2: Index Test (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

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Stokes 2021(a) [A] *(Continued)*

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Stokes 2021(a) [B]
Study characteristics

Patient Sampling Comparative study of 3 sample types; [Stokes 2021\(a\) \[A\]](#) details the full study characteristics and QUADAS.

Patient characteristics and setting Comparative study of 3 sample types; [Stokes 2021\(a\) \[A\]](#) details the full study characteristics and QUADAS.

Index tests

Test name: Panbio

Manufacturer: Abbott, IL, USA

Antibody: nucleocapsid

Ag target: not stated

Test method: CGIA

Samples used: [A] NP, **[B] OP**, [C], saliva
 [A] and **[B] collected by trained HCWs**, [C] was self-collected using ClassiqSwab
 Paired NP swabs collected from separate nostrils; OP swabs collected from both sides of the oropharynx and the posterior pharyngeal wall under the uvula
[B] and [C] sampling was terminated early due to poor sensitivity compared to NP

Stokes 2021(a) [B] *(Continued)*

	Transport media: none used; tested immediately Sample storage: no storage Test operator: states tested immediately, so presume same HCW Definition of test positivity: visual line Blinding reported: yes (conducted first); but not blinded to COVID-19 status (all previously PCR+) Timing of samples: mean duration of symptoms 6.1 d (median 6.0, range 3.0–10.0 d); 91% were ≤ 7 d pso
Target condition and reference standard(s)	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.

Stokes 2021(a) [C]
Study characteristics

Patient Sampling	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.
Index tests	Test name: Panbio Manufacturer: Abbott, IL, USA Antibody: nucleocapsid Ag target: not stated Test method: CGIA Samples used: [A] NP, [B] OP, [C] saliva [A] and [B] collected by trained HCWs, [C] was self-collected using ClassiqSwab Paired NP swabs collected from separate nostrils; OP swabs collected from both sides of the oropharynx and the posterior pharyngeal wall under the uvula [B] and [C] sampling was terminated early due to poor sensitivity compared to NP Transport media: none used; tested immediately Sample storage: no storage Test operator: states tested immediately, so presume same HCW Definition of test positivity: visual line Blinding reported: yes (conducted first); but not blinded to COVID-19 status (all previously PCR+) Timing of samples: mean duration of symptoms 6.1 d (median 6.0, range 3.0–10.0 d); 91% were ≤ 7 d pso

Stokes 2021(a) [C] *(Continued)*

Target condition and reference standard(s)	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 3 sample types; Stokes 2021(a) [A] details the full study characteristics and QUADAS.

Stokes 2021(b)
Study characteristics

Patient Sampling	<p>Report of 3 studies estimating sensitivity and/or specificity</p> <p>(1) Sensitivity only: symptomatic participants with a recent positive SARS-CoV-2 PCR were invited to contribute further samples for an RDT evaluation; only those who were still PCR +ve on paired swabs are included (Stokes 2021(a) [A])</p> <p>(2) Sensitivity and specificity: symptomatic individuals presenting to Alberta Health Services community COVID-19 assessment centres within 7 d of symptom(s) onset (Stokes 2021(b))</p> <p>Excluded from review: (3) Specificity only: panel of samples from asymptomatic individuals at low risk of having COVID-19 (all PCR-ve) and retrospective samples containing various respiratory viruses</p> <p>Recruitment: not specifically stated but all attending who met the criteria were invited to participate</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): (2) 1641 (268)</p>
Patient characteristics and setting	<p>Setting: community COVID-19 test centre</p> <p>Location: Alberta Health Services community COVID-19 assessment centres in Edmonton and Calgary</p> <p>Country: Canada</p> <p>Dates: not stated</p> <p>Symptoms and severity: all symptomatic; no further details</p> <p>Demographics: mean age 40.8 years (median 39.0 years, range 5.0-90.0 years); 40.0% male</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Panbio</p> <p>Manufacturer: Abbott, IL, USA</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: NP; collected by Alberta Health Services nurses</p> <p>Transport media: none used; tested immediately</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Stokes 2021(b) (Continued)

	<p>Sample storage: no storage</p> <p>Test operator: states tested immediately, so presume same nurse</p> <p>Definition of test positivity: visual line</p> <p>Blinding reported: yes (conducted first)</p> <p>Timing of samples: not reported; all < 7 days</p>
Target condition and reference standard(s)	<p>Reference standard: PCR; APL E-gene PCR or a Health Canada/FDA-approved commercial assay according to site (Allplex (Seegene, Seoul, South Korea), BDMax (Becton Dickinson, NJ, USA), Panther Fusion (Hologic, MA, USA), GeneXpert (Cepheid, CA, USA), or Simplexa (DiaSorin, Saluggia, Italy)). Discrepant results (FPs) were re-extracted and retested in triplicate with the N2 assay from the US CDC 2019–Novel Coronavirus (2019-nCoV) real-time PCR diagnostic panel</p> <p>Definition of non-COVID cases: single negative</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP in UTM (n = 1551, 94.5%); OP in UTM (n = 90, 5.5%)</p> <p>Timing of reference standard: as for index</p> <p>Blinded to index test: not stated</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: 'funded using internal operating funds of Alberta Precision Laboratories and Alberta Health Services. Test kits and instruments were paid for by the Public Health Agency of Canada.'</p> <p>Publication status: published</p> <p>Source: European Journal of Clinical Microbiology & Infectious Diseases</p> <p>Author COI: the authors declare that they have no conflict of interest.</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Stokes 2021(b) *(Continued)*

Was a case-control design avoided?	Yes	
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Stokes 2021(b) *(Continued)*

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Stromer 2020
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity only: upper respiratory tract samples (also described as "deep nasopharyngeal swabs") pre-characterized by a positive or negative RT-PCR result (Ag results not reported for PCR- samples)</p> <p>Recruitment: not mentioned; implies deliberate sampling to ensure samples with a range of Ct values were included</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 134 (124); subgroup of 21 PCR+ve samples used to compare 2 Ag tests not included</p>
Patient characteristics and setting	<p>Setting: unclear</p> <p>Location: Institute for Infection Medicine, Christian-Albrecht University and University Medical Center, Schleswig-Holstein</p> <p>Country: Germany</p> <p>Dates: not stated</p> <p>Symptoms and severity: not stated</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: NADAL COVID-19 Ag Test (A second test used on selected subgroup of samples was not included; Abbott Panbio COVID-19 Antigen rapid test)</p> <p>Manufacturer: Nal von Minden GmbH</p> <p>Antibody: nucleoprotein</p> <p>Ag target: not stated</p> <p>Test method: unknown</p> <p>Samples used: NP</p> <p>Transport media: 500 µL of sterile PBS</p> <p>Sample storage: not stated</p>

Stromer 2020 (Continued)

	<p>Test operator: not stated</p> <p>Definition of test positivity: not stated</p> <p>Blinding reported: assume no?, conducted after RT-PCR and states "all samples were pre-characterized by a positive or a negative result"</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; in-house</p> <p>Definition of non-COVID cases: single negative PCR</p> <p>Genetic target(s): N gene</p> <p>Samples used: NP; same samples as index test</p> <p>Timing of reference standard: unclear</p> <p>Blinded to index test: yes, conducted first</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same swab</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "financial support by DFG (German Research Foundation) within the funding programme Open Access Publizieren"</p> <p>Publication status: published</p> <p>Source: Microorganisms</p> <p>Author COI: 'the authors declare no conflict of interest. The Nal von Minden GmbH supported this study by providing free kits and a scanner for optical intensity measurement. This company had no influence on the writing of the manuscript or on the interpretation of the data'</p>

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 inclusions?	Unclear		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Stromer 2020 (Continued)

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 (Evaluations of single test application)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
If a threshold was used, was it pre-specified?	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?	High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)	
DOMAIN 3: Reference Standard	
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes

Stromer 2020 (Continued)

Could the patient flow have introduced bias?

Unclear risk

Takeda 2020
Study characteristics

Patient Sampling	<p>2-group study to estimate sensitivity and specificity, in:</p> <p>[1] RT-PCR+ve confirmed COVID-19 samples selected from a total of 88 positive samples during time period (n = 62)</p> <p>[2] random sample of RT-PCR-ve samples selected from 1363 negative specimens tested during same time frame (n = 100)</p> <p>Recruitment: unclear for cases (may have been all "initial" samples tested); random sample of non-cases</p> <p>Prospective or retrospective: unclear</p>
Patient characteristics and setting	<p>Setting: not stated; multiple clinical institutions</p> <p>Location: SRL Inc, Tokyo</p> <p>Country: Japan</p> <p>Dates: "early April" also later states 4-day period</p> <p>Symptoms and severity: not stated</p> <p>High viral load (< 25 Ct) 32/60, 53%</p> <p>Low viral load (≥ 25 Ct) 28/60, 47%</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: ESPLINE SARS-CoV-2 (no product code reported)</p> <p>Manufacturer: Fujirebio Inc</p> <p>Antibody: SARS-CoV-2 Ag (from IFU)</p> <p>Ag target: anti-SARS-CoV-2 monoclonal antibodies (mouse) (from IFU)</p> <p>Test method: LFA using ALP-labelled antibodies</p> <p>Samples used: NP; collection not reported</p> <p>Transport media: not described</p> <p>Sample storage: swabs mixed with sample treatment solution; no storage reported</p> <p>Test operator: not stated; laboratory staff presumed</p> <p>Definition of test positivity: visual line, as per manufacturer IFU</p> <p>Blinding reported: not stated</p> <p>Timing of samples: not stated but all cases are first samples presumed by authors to be from patient suspected of SARS-CoV-2 for the first time; negative samples were "probably ... from ... COVID-19 patients for monitoring purposes and to check for negative conversion"</p>

Takeda 2020 (Continued)

Target condition and reference standard(s)	Reference standard: RT-PCR; QuantiTect Probe RT-PCR Kit (Qiagen) Definition of non-COVID cases: as for cases; single negative required Genetic target(s): N2 Samples used: NP, as for index test Timing of reference standard: not stated Blinded to index test: not stated Incorporated index test: no
Flow and timing	Time interval between index and reference tests: simultaneous, same samples All participants received same reference standard: yes Missing data: 16 positive samples omitted; possibly because not initial samples but unclearly reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant (for cases), not clear for non-cases
Comparative	
Notes	Funding: none reported, however laboratory wholly owned by test manufacturer Publication status: preprint Source: medRxiv Author COI: "SRL Inc. is a subsidiary of Miraca Holdings Inc. Miraca Holdings Inc. holds all stock of Fujirebio Inc."

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?	No		
Did the study avoid inappropriate inclusions?	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

Takeda 2020 (Continued)

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Takeuchi 2021a
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: participants referred to a drive-through PCR testing centre from 1 of 3 groups:</p> <ol style="list-style-type: none"> 1. primary care facilities (n = 1151 from 89 centres) 2. from a local public health centre (n = 928) 3. health workers from the study hospital (n = 45) <p>Recruitment: not stated; appears to be all who accepted invitation to participate during study period</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 1186 (105) included from a total of 2079 referred patients and HCWs</p>
Patient characteristics and setting	<p>Setting: primary care COVID-testing facility</p> <p>Location: PCR centre in Tsukuba Medical Center Hospital</p> <p>Country: Japan</p> <p>Dates: 7 October-5 December 2020</p> <p>Symptoms and severity: 771, 65% symptomatic, 415, 35% asymptomatic; fever (617, 80%), cough/sputum production (294, 38.1%), runny nose/nasal congestion (196, 25.4%), loss of taste or smell (33, 4.3%), dyspnoea (6, 0.8%), fatigue (77, 10%), diarrhoea (44, 5.7%), sore throat (149, 19.3%), headache (83, 10.8%)</p> <p>Demographics: median age 36.5 years, IQR 23-50 years; 647 male (54.6%)</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: QuickNavi COVID-19 Ag</p> <p>Manufacturer: Denka Co., Ltd., Tokyo, Japan</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: lateral flow, no further details</p> <p>Samples used: NP; collection not reported but states samples were "obtained"</p> <p>Transport media: none used; sample buffer solution only</p> <p>Sample storage: immediate, no storage</p> <p>Test operator: not stated; states "examiner"</p> <p>Definition of test positivity: visual interpretation</p> <p>Blinding reported: yes done immediately after sample collection</p> <p>Timing of samples: median days from symptoms onset 2, IQR 1-4</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; in-house at microbiology laboratory located next to the drive-through sample-collecting place of the PCR centre within an hour; samples also tested at reference laboratory using assay developed by the National Institute of Infectious Diseases, Japan, samples discrepant between the 2 PCRs were tested using BioFire Respiratory Panel 2.1 and FilmArray systems (BioFire Diagnostics, LLC, UT, USA)</p> <p>Definition of non-COVID cases: double negative for absence of infection</p>

Takeuchi 2021a (Continued)

	Genetic target(s): not stated Samples used: NP in UTM Timing of reference standard: not stated Blinded to index test: unclear Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same time; paired swabs All participants received same reference standard: yes Missing data: 4 excluded due to missing symptom status Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): there was 1 discordant sample that was positive on in-house RT-PCR and negative on reference real-time RT-PCR. Considered negative after additional BioFire Respiratory Panel 2.1 examination Unit of analysis: participant
Comparative	
Notes	Funding: not stated Publication status: preprint Source: not stated Author COI: "Denka Co., Ltd., provided fees for research expenses and the QuickNavi-COVID19 Ag kits without charge. Hironichi Suzuki received a lecture fee from Otsuka Pharmaceutical Co., Ltd., regarding this study. Daisuke Kato, Miwa Kuwahara and Shino Muramatsu belong to Denka Co., Ltd., the developer of the QuickNavi-COVID19 Ag"

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 inclusions?	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 (Evaluations of single test application)			

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Takeuchi 2021a (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Low risk

Takeuchi 2021b

Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: participants referred to a drive-through PCR centre from a local public health centre or from one of 97 primary care facilities; also states 17 samples obtained during hospitalization</p> <p>Recruitment: not stated; appears to include all meeting eligibility criteria at testing centre but also includes hospitalized</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 862 (51)</p>
Patient characteristics and setting	<p>Setting: mainly COVID-19 testing centre</p> <p>Location: not stated; multiple institutions in Tsukuba, Ibaraki</p> <p>Country: Japan</p> <p>Dates: 7 October 2020-9 January 2021</p> <p>Symptoms and severity: 790, 91.6% symptomatic; most commonly reported included fever (628, 79.5%), cough or sputum production (255, 32.3%), sore throat (210, 26.6%), runny nose or nasal congestion (185, 23.4%), headache (121, 15.3%). Loss of taste or smell (was reported in 32 (4.1%) overall and in 14 (27.5%) of PCR+ve group 72 (8.4%) asymptomatic</p> <p>Demographics: median age 36.0 years (IQR 24.0-48.0); 106 (12.3%) were < 18 years; 383 (44.4%) female</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: QuickNavi-COVID19 Ag</p> <p>Manufacturer: Denka Co., Ltd., Tokyo, Japan</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: AN; collection appears to be by staff using FLOQswab</p> <p>Transport media: not used</p> <p>Sample storage: none; tested immediately</p> <p>Test operator: not stated; "examiner"</p> <p>Definition of test positivity: visual interpretation</p> <p>Blinding reported: yes; done first</p> <p>Timing of samples: median 2 d pso (IQR 1.0-3.0)</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR;</p> <ol style="list-style-type: none"> in-house LDT for diagnosis (in-house microbiology laboratory located next to the drive-through samples were then stored at -80 °C and tested weekly using a reference real-time RT-PCR QuantiTect Probe RT-PCR Kit (QIAGEN Inc., Germantown, MD, USA)

Takeuchi 2021b (Continued)

3. discrepant samples testing using Xpert Xpress (Cepheid Inc)

Definition of non-COVID cases: single negative

Genetic target(s): not reported for in-house assay; N and N2 for Quantitect

Samples used: NP in UTM

Timing of reference standard: as for index

Blinded to index test: unclear

Incorporated index test: not reported for in-house assay; N and N2 for Quantitect

Flow and timing

Time interval between index and reference tests: simultaneous; paired (NP collected after AN swab)

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): 1 sample was discrepant between LDT (+ve) and Quantitect assay (-ve); +ve Xpert Xpress (Ct 39.8 on N2)
 Sample was obtained from a participant who had been diagnosed with COVID-19 1 month before the current evaluation and who was referred to the PCR centre due to refractory respiratory symptoms

Unit of analysis: participant

Comparative

Notes

Funding: "Denka Co., Ltd., provided fees for research expenses and the QuickNavi-COVID19 Ag kits without charge"

Publication status: preprint

Source: medRxiv

Author COI: "Hiromichi Suzuki received a lecture fee from Otsuka Pharmaceutical Co. Ltd., regarding this study. Daisuke Kato, Miwa Kuwahara and Shino Muramatsu belong to Denka Co., Ltd., the developer of the QuickNavi COVID19 Ag"

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 inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Takeuchi 2021b (Continued)

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Takeuchi 2021b (Continued)

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Thommes 2021 [A]
Study characteristics

Patient Sampling

Single-group study to estimate sensitivity alone: consecutive COVID-19 patients admitted to the inpatient ward at the Department of Internal Medicine; described as moderate to severe disease

Recruitment: consecutive

Prospective or retrospective: prospective

Sample size (cases): 154 (154)

Patient characteristics and setting

Setting: inpatient

Location: Department of Internal Medicine II, the Medical University of Innsbruck

Country: Austria

Dates: August to end October 2020

Symptoms and severity: moderate to severe; all admitted

Demographics: median age 69 years (range 18–92), 35.7% women

Exposure history: not stated

Index tests

Test name: **[A] Panbio™ COVID-19 Ag Rapid test**
 [B] Novel Coronavirus (2019-nCov) Antigen Detection Kit
 [C] DIAQUICK COVID-19 Ag Cassette
 [D] SARS-CoV-2 Rapid Antigen Test

Manufacturer: **[A] Abbott, Chicago, Illinois**
 [B] CLMSRDL, Sichuan Mass Spectrometry Biotechnology Co., Ltd, Chengdu, Sichuan
 [C] DIALAB, Wiener Neudorf, Austria
 [D] Roche Diagnostics Deutschland GmbH, Mannheim, Germany

Antibody: not stated

Ag target: not stated

Test method: LFA

Samples used: NP; collected by expert staff

Transport media: none used

Sample storage: none

Test operator: performed by expert staff at the bedside using swabs provided in the Ag test kits

Definition of test positivity: visual line

Thommes 2021 [A] (Continued)

	Blinding reported: yes, done first
	Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR; using Cobas apparatus (Roche Diagnostics GmbH, Mannheim, Germany)
	Definition of non-COVID cases: single negative
	Genetic target(s): target ORF1a/b and B-CoV target E-Gene
	Samples used: OP
	Timing of reference standard: same as for index
	Blinded to index test: not stated
	Incorporated index test: not stated
Flow and timing	Time interval between index and reference tests: paired; simultaneous
	All participants received same reference standard: yes
	Missing data: yes; 145 patients reportedly recruited but number for samples per assay varied from 71-99. No reason for missing data was given
	Uninterpretable results: unclear
	Indeterminate results (index test): unclear
	Indeterminate results (reference standard): unclear
	Unit of analysis: participant
Comparative	
Notes	Funding: there was no funding source for this study
	Publication status: published
	Source: International Journal of Infectious Diseases
	Author COI: no known competing financial interests or personal relationships

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?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	

Thommes 2021 [A] (Continued)

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Thommes 2021 [B]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name: [A] PanbioTM COVID-19 Ag Rapid test [B] Novel Coronavirus (2019-nCov) Antigen Detection Kit [C] DIAQUICK COVID-19 Ag Cassette [D] SARS-CoV-2 Rapid Antigen Test</p> <p>Manufacturer: [A] Abbott, Chicago, Illinois [B] CLMSRDL, Sichuan Mass Spectrometry Biotechnology Co., Ltd, Chengdu, Sichuan [C] DIALAB, Wiener Neudorf, Austria [D] Roche Diagnostics Deutschland GmbH, Mannheim, Germany</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: LFA</p> <p>Samples used: NP; collected by expert staff</p> <p>Transport media: none used</p> <p>Sample storage: none</p> <p>Test operator: performed by expert staff at the bedside using swabs provided in the Ag test kits</p> <p>Definition of test positivity: visual line</p> <p>Blinding reported: yes, done first</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.

Thommes 2021 [C]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name: [A] PanbioTM COVID-19 Ag Rapid test [B] Novel Coronavirus (2019-nCov) Antigen Detection Kit [C] DIAQUICK COVID-19 Ag Cassette</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Thommes 2021 [C] *(Continued)*

[D] SARS-CoV-2 Rapid Antigen Test

Manufacturer: [A] Abbott, Chicago, Illinois

[B] CLMSRDL, Sichuan Mass Spectrometry Biotechnology Co., Ltd, Chengdu, Sichuan

[C] DIALAB, Wiener Neudorf, Austria

[D] Roche Diagnostics Deutschland GmbH, Mannheim, Germany

Antibody: not stated

Ag target: not stated

Test method: LFA

Samples used: NP; collected by expert staff

Transport media: none used

Sample storage: none

Test operator: performed by expert staff at the bedside using swabs provided in the Ag test kits

Definition of test positivity: visual line

Blinding reported: yes, done first

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.

Thommes 2021 [D]
Study characteristics

Patient Sampling	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Patient characteristics and setting	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Index tests	<p>Test name: [A] PanbioTM COVID-19 Ag Rapid test [B] Novel Coronavirus (2019-nCov) Antigen Detection Kit [C] DIAQUICK COVID-19 Ag Cassette [D] SARS-CoV-2 Rapid Antigen Test</p> <p>Manufacturer: [A] Abbott, Chicago, Illinois [B] CLMSRDL, Sichuan Mass Spectrometry Biotechnology Co., Ltd, Chengdu, Sichuan [C] DIALAB, Wiener Neudorf, Austria [D] Roche Diagnostics Deutschland GmbH, Mannheim, Germany</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p>

Thommes 2021 [D] *(Continued)*

Test method: LFA

Samples used: NP; collected by expert staff

Transport media: none used

Sample storage: none

Test operator: performed by expert staff at the bedside using swabs provided in the Ag test kits

Definition of test positivity: visual line

Blinding reported: yes, done first

Timing of samples: not stated

Target condition and reference standard(s)	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Flow and timing	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.
Comparative	
Notes	Comparative study of 4 Ag tests; Thommes 2021 [A] details the full study characteristics and QUADAS.

Toptan 2021(a)
Study characteristics

Patient Sampling	<p>Report of 2 single-group studies to estimate sensitivity and specificity: [1] samples stored after routine diagnostic use (Institute of Virology, Charite Berlin) (Toptan 2021(a)) [2] clinical samples collected as part of registered protocols from individuals living in shared housing (Institute of Virology, Frankfurt) (included as Toptan 2021(b))</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: [1] retrospective (frozen samples)</p> <p>Sample size (cases): [1] 67 (58)</p>
Patient characteristics and setting	<p>Setting: unclear</p> <p>Location: [1] Institute of Virology, Charite Berlin</p> <p>Country: Germany</p> <p>Dates: not stated</p> <p>Symptoms and severity: not stated</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: not stated (may be RIDA-QUICK SARS-CoV-2 Antigen assay)</p> <p>Manufacturer: R-Biopharm</p> <p>Antibody: not stated</p>

Toptan 2021(a) *(Continued)*

	<p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: [1] combined OP + NP</p> <p>Transport media: [1] after thawing at room temperature, swabs were resuspended in 1.5 mL of PBS</p> <p>Sample storage: stored (frozen) samples used</p> <p>Test operator: not stated</p> <p>Definition of test positivity: evaluated visually with 4 or 6 eye principle</p> <p>Blinding reported: yes, done in parallel (not sure this means blinded?)</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR</p> <p>Definition of non-COVID cases:</p> <p>Genetic target(s): ORF1 and E gene</p> <p>Samples used: [1] combined OP + NP</p> <p>Timing of reference standard: not stated</p> <p>Blinded to index test: done in parallel (not sure this means blinded?)</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same samples</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "part of this work was funded by the German Ministry of Health (Konsiliarlabor für Coronaviren) to CD and VMC and by the German Ministry of Research through projects VARIPath (01KI2021)to VMC. This project was funded in part by the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) (NaFoUniMedCovid19 – B-FAST, EVIPAN, FKZ:01KX202)"</p> <p>Publication status: published</p> <p>Source: Journal of Clinical Virology</p> <p>Author COI: "no known competing financial interests or personal relationships"</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Toptan 2021(a) *(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 inclusions?	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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes	
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Toptan 2021(a) *(Continued)*

Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Toptan 2021(b)
Study characteristics

Patient Sampling	<p>Report of 2 single-group studies to estimate sensitivity and specificity: [1] samples stored after routine diagnostic use (Institute of Virology, Charite Berlin) (included as Toptan 2021(a)) [2] clinical samples collected as part of registered protocols from individuals living in shared housing (Institute of Virology, Frankfurt) (Torres 2021b)</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: [2] unclear</p> <p>Sample size (cases): [2] 70 (32)</p>
Patient characteristics and setting	<p>Setting: unclear</p> <p>Location: [2] Institute of Virology, Frankfurt</p> <p>Country: Germany</p> <p>Dates: not stated</p> <p>Symptoms and severity: not stated</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: not stated (may be RIDA-QUICK SARS-CoV-2 Ag assay)</p> <p>Manufacturer: R-Biopharm</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: not stated</p> <p>Samples used: [2] NP</p> <p>Transport media: [2] 2 mL of PBS</p> <p>Sample storage: [2] Stored at 4 °C, processed within 24 h</p> <p>Test operator: not stated</p> <p>Definition of test positivity: evaluated visually with 4 or 6 eye principle</p>

Toptan 2021(b) (Continued)

	Blinding reported: yes, done in parallel
	Timing of samples: not stated
Target condition and reference standard(s)	Reference standard: RT-PCR Definition of non-COVID cases: Genetic target(s): ORF1 and E gene Samples used: [2] NP Timing of reference standard: not stated Blinded to index test: done in parallel (not sure this means blinded?) Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same samples All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: 'parts of this work was funded by the German Ministry of Health (Konsiliarlabor für Coronaviren) to CD and VMC and by the German Ministry of Research through projects VARIPath (01KI2021) to VMC. This project was funded in part by the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) (NaFoUniMedCovid19 – B-FAST, EVIPAN, FKZ:01KX202)' Publication status: published Source: Journal of Clinical Virology Author COI: "no known competing financial interests or personal relationships"

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 inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Toptan 2021(b) *(Continued)*

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

DOMAIN 2: Index Test (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Torres 2021a

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: asymptomatic household (n = 338) or non-household (n = 296) close contacts of COVID-19 patients as defined by the Spanish Ministry of Health (i.e. presence of compatible signs or symptoms and a positive NP swab RT-PCR)</p> <p>Recruitment: consecutive</p> <p>Prospective or retrospective: prospective</p> <p>Sample size (cases): 634 (79)</p>
Patient characteristics and setting	<p>Setting: contact tracing</p> <p>Location: Clínico-Malvarrosa Health Department, Valencia</p> <p>Country: Spain</p> <p>Dates: 16 October-20 November 2020</p> <p>Symptoms and severity: all asymptomatic; 39/79 PCR+ve individuals subsequently developed mild symptoms</p> <p>Demographics: male: 279 (44%), median age 37 years; range, 9-87 years</p> <p>Exposure history: all contacts of confirmed cases; 338/634 were household contacts</p>
Index tests	<p>Test name: Panbio COVID-19 Ag Rapid Test Device</p> <p>Manufacturer: Abbott (Diagnostic GmbH, Jena, Germany)</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: lateral flow, no further information</p> <p>Samples used: NP (collected by experienced nurses)</p> <p>Transport media: none used</p> <p>Sample storage: immediate, no storage</p> <p>Test operator: not stated; may be same nurse "carried out at POC immediately after sampling"</p> <p>Definition of test positivity: not stated; as per manufacturer IFU</p> <p>Blinding reported: yes done first</p> <p>Timing of samples: timing was prescribed at the discretion of either the physician in charge of the index case or local health authorities:</p> <ul style="list-style-type: none"> • household contacts - median 2 d (range, 1-7 d) after diagnosis of the presumed index case • non-household contacts - median 6 d (range, 1-7 d) after self-reported exposure
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, MA, USA)</p> <p>Definition of non-COVID cases: single negative</p> <p>Genetic target(s): N gene</p>

Torres 2021a (Continued)

Samples used: NP in 3 mL of UTM (Becton Dickinson, Sparks, MD, USA)

Timing of reference standard: as for index test

Blinded to index test: unclear

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired swab from alternative nostril

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: "this work received no public or private funds. Abbott Diagnostics provided the Panbio"
 COVID-19 Ag Rapid Test Device kits.

Publication status: published

Source: Clinical Microbiology and Infection

Author COI: the authors declare 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Torres 2021a (Continued)

If a threshold was used, was it pre-specified? 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 (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Torres 2021b
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity: appears to include participants meeting COVID-19 testing criteria, described as either

Torres 2021b (Continued)

1. outpatients with suspected COVID-19 with ≤ 5 days symptoms (≥ 1 of: fever, dry cough, rhinorrhoea, chest pain, dyspnoea, myalgia, fatigue, anosmia, ageusia, odynophagia, diarrhoea, conjunctivitis, and cephalgia)
2. asymptomatic close contacts of COVID-19 patients (household or non-household) as defined by the Spanish Ministry of Health

Recruitment: unclear

Prospective or retrospective: prospective

Sample size (cases): 270 (106)

Patient characteristics and setting

Setting: outpatients

Unclear but could class as COVID-19 test centre (acknowledgments mention Ag testing in primary healthcare centres, so may be anyone meeting testing criteria)

Location: not reported. Authors affiliated to Hospital Clínico Universitario, INCLIVA Research Institute, Valencia

Country: Spain

Dates: 26 November 2020-21 January 2021

Symptoms and severity: mixed; 178 (66%) symptomatic

Demographics: symptomatic COVID-19 suspects: median age (range): 41 (11-83) years

Sex: 112/178 (63%) female

Asymptomatic COVID-19 contacts: median age (range): 44 (11-87) years

Sex: 54/92 (59%) female

Exposure history: 78 household contacts

14 non-household contacts

Index tests

Test name: CLINITEST Rapid COVID-19 Antigen Test (reported elsewhere to be the same as the Healgen Coronavirus Ag Rapid Test Cassette)

Manufacturer: Siemens, Healthineers, Erlangen, Germany

Antibody: SARS-CoV-2 nucleocapsid protein

Ag target: not reported

Test method: not reported

Samples used: NP left nostril (experienced nurses)

Transport media: none

Sample storage: immediate testing

Test operator: not reported; appears to be same nurse

Definition of test positivity: according to manufacturer

Blinding reported: yes; conducted first

Timing of samples: median (range) pso or post diagnosis of index case: symptomatic 3 (1-5) d

Asymptomatic household contacts 4 (0-7) d

Asymptomatic non-household contacts 5 (2-7) d

Target condition and reference standard(s)

Reference standard: RT-PCR; Taq-Path COVID-19 Combo Kit (ThermoFisher Scientific, Massachusetts, USA)

Torres 2021b (Continued)

Definition of non-COVID cases: same as for cases

Genetic target(s): not reported

Samples used: NP right nostril, placed in 3 mL of UTM, Becton Dickinson, Sparks, MD, USA)

Timing of reference standard: same as for index test

Blinded to index test: not reported

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: simultaneously; paired swabs

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: this work received no public or private funds; "Siemens Healthineers provided the Rapid Test Device kits, but the company had no role in the study design, data collection, data analysis, data interpretation, or writing of the report"

Publication status: published letter

Source: Journal of Infection

Author COI: the authors declare 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 inclusions?	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 (Evaluations of single test application)			

Torres 2021b (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Turcato 2021
Study characteristics

Patient Sampling	<p>Single-group study estimating sensitivity and specificity: all patients with symptoms suspicious for SARS-CoV-2 infection, with a temperature > 37.3 °C, with any epidemiological risk criteria (e.g. reported contact with an infected person) or evaluated in the ED for other conditions not related to SARS-CoV-2 infection that required hospitalization</p> <p>Recruitment: consecutive; "all" included</p> <p>Prospective or retrospective: not stated; appears prospective</p> <p>Sample size (cases): 3410 (223)</p>
Patient characteristics and setting	<p>Setting: ED</p> <p>Location: Hospital of Merano (SABES-ASDAA), Merano-Meran</p> <p>Country: Italy</p> <p>Dates: 1 July-10 November 2020</p> <p>Symptoms and severity: 991, 29% symptomatic; 2419, 71% asymptomatic</p> <p>Demographics: not reported</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: STANDARD Q COVID-19 Ag (R-Ag) kit</p> <p>Manufacturer: SD BIOSENSOR, KR</p> <p>Antibody: not stated</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: not reported; states "two swabs"</p> <p>Transport media: not reported; presume none used</p> <p>Sample storage: not reported; states "implementation ... in the initial screening"</p> <p>Test operator: not reported</p> <p>Definition of test positivity: not reported; as per manufacturer IFU</p> <p>Blinding reported: not stated; appear to have been conducted first</p> <p>Timing of samples: not stated</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; no details provided</p> <p>Definition of non-COVID cases: as for cases (single negative PCR)</p> <p>Genetic target(s): not reported</p> <p>Samples used: not stated; paired "swabs" implied</p> <p>Timing of reference standard: not stated</p> <p>Blinded to index test: not stated</p>

Turcato 2021 (Continued)

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: not stated; paired "swabs" implied

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: participant

Comparative

Notes

Funding: no funding statement provided

Publication status: published letter

Source: Journal of Infection

Author COI: no COI statement provided

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			Unclear

Turcato 2021 (Continued)

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? Unclear risk

Van der Moeren 2021(a) [A]
Study characteristics

Patient Sampling	<p>Study reports data for 2 cohorts. Van der Moeren 2021(a) [A] relates to cohort [1] single-group study to estimate sensitivity and specificity: all adults presenting at a single community test centre for COVID-19 testing (n = 354) See Van der Moeren 2021(b) for cohort [2] data</p> <p>[2] Single-group study to estimate sensitivity alone: patients with a positive PCR test result at 1 of 3 community testing facilities who were retested at home within 72 h of initial positive result (n = 132)</p> <p>Recruitment: consecutive; "all" adults invited to participate</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: COVID-19 test centre (community)</p> <p>Location: Municipal Health Service (GGD) regional test centre at Breda</p> <p>Country: Netherlands</p>

Van der Moeren 2021(a) [A] (Continued)

Dates: 28-30 September
Symptoms and severity: not stated; symptomatic
Demographics: not stated
Exposure history: not stated

Index tests

Test name: BD Veritor System for Rapid Detection of SARS-CoV-2
Manufacturer: Becton Dickinson
Antibody: NP
Ag target: not stated
Test method: LFA; no further detail
Samples used: NOP; "specimen from the throat and the superficial nasal cavities (bilateral, 2.5 cm proximal from the nostril)"; collected by GGD employee
Transport media: direct testing
Sample storage: stored dry in sterile test tubes and stored and transported on dry ice until processing at the laboratory; tested within 6 h after collection
Test operator: trained laboratory technicians
Definition of test positivity: **[A] results reported using analyser device** and [B] results by naked eye inspection alone (visual)
Blinding reported: not stated
Timing of samples: not reported; on presentation
Time pso only provided for PCR+ve cases: 12 < 7 d; 1 ≥ 7 d; 4 = no pso data

Target condition and reference standard(s)

Reference standard: RT-PCR; either Cobas 6800 (Roche) or the m2000 (Abbott)
Definition of non-COVID cases: as for cases; single negative
Genetic target(s): E- and RDRP-gene (Cobas) or E-gene and N-gene (Abbott)
Samples used: NOP; specimen from the throat and nasal cavity up to the nasal bridge
Timing of reference standard: as for index test
Blinded to index test: not stated
Incorporated index test: no

Flow and timing

Time interval between index and reference tests: paired
All participants received same reference standard: yes; different assays
Missing data: 2 samples excluded due to RT-PCR coding error (considered overall low risk of bias due to small numbers)
Uninterpretable results: 1 invalid on Ag test
Indeterminate results (index test): none reported
Indeterminate results (reference standard): none reported
Unit of analysis: participant

Van der Moeren 2021(a) [A] (Continued)

Comparative

Notes

Funding: "the VRD (Ag) tests for this study were provided by the Dutch Ministry of Health, Welfare and Sport (VWS)"

Publication status: preprint

Source: medRxiv

Author COI: "Jan Kluytmans is member of the National Outbreak Management Team of The Netherlands and of a committee which supports the implementation of the Corona-reporting App."

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		

Van der Moeren 2021(a) [A] *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Low risk

Van der Moeren 2021(a) [B]
Study characteristics

Patient Sampling	Study compares test interpretation using an analyzer (Van der Moeren 2021(a) [A]) with interpretation by naked eye (Van der Moeren 2021(a) [B]); Van der Moeren 2021(a) [A] reports full study characteristics and QUADAS.
Patient characteristics and setting	Study compares test interpretation using an analyzer (Van der Moeren 2021(a) [A]) with interpretation by naked eye (Van der Moeren 2021(a) [B]); Van der Moeren 2021(a) [A] reports full study characteristics and QUADAS.
Index tests	Study compares test interpretation using an analyzer (Van der Moeren 2021(a) [A]) with interpretation by naked eye (Van der Moeren 2021(a) [B]); Van der Moeren 2021(a) [A] reports full study characteristics and QUADAS.
Target condition and reference standard(s)	Study compares test interpretation using an analyzer (Van der Moeren 2021(a) [A]) with interpretation by naked eye (Van der Moeren 2021(a) [B]); Van der Moeren 2021(a) [A] reports full study characteristics and QUADAS.

Van der Moeren 2021(a) [B] *(Continued)*

Flow and timing Study compares test interpretation using an analyzer ([Van der Moeren 2021\(a\) \[A\]](#)) with interpretation by naked eye ([Van der Moeren 2021\(a\) \[B\]](#)); [Van der Moeren 2021\(a\) \[A\]](#) reports full study characteristics and QUADAS.

Comparative

Notes

Van der Moeren 2021(b)

Study characteristics

Patient Sampling	<p>Study reports data for 2 cohorts:</p> <p>Van der Moeren 2021(b) relates to cohort [2]: single-group study to estimate sensitivity alone: patients with a positive PCR test result at 1 of 2 community testing facilities who were retested at home within 72 h of initial positive result (n = 132)</p> <p>See Van der Moeren 2021(a) [A] for data related to cohort [1]: single-group study to estimate sensitivity and specificity: all adults presenting at a single community test centre for COVID-19 testing (n = 354)</p> <p>Recruitment: unclear; implies "all" those with positive PCR invited to participate</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: community</p> <p>Location: Municipal Health Service (GGD) regional test centres at Breda or Roosendaal</p> <p>Country: Netherlands</p> <p>Dates: 28 September-6 October</p> <p>Symptoms and severity: at time of home visit: asymptomatic 3, 2% (2/3 still PCR+ve) Symptomatic 129 (123 still PCR+ve) Day < 7 66, 50% Day > 7 57, 43%</p> <p>Demographics: not stated</p> <p>Exposure history: not stated</p>
Index tests	<p>Test name: BD Veritor System for Rapid Detection of SARS-CoV-2</p> <p>Manufacturer: Becton Dickinson</p> <p>Antibody: NP</p> <p>Ag target: not stated</p> <p>Test method: LFA; no further detail</p> <p>Samples used: NOP? "specimen from the throat and the superficial nasal cavities (bilateral, 2.5 cm proximal from the nostril)"; collected by GGD employee</p> <p>Transport media: direct testing</p> <p>Sample storage: stored dry in sterile test tubes and stored and transported on dry ice until processing at the laboratory; tested within 6 h after collection</p> <p>Test operator: trained laboratory technicians</p>

Van der Moeren 2021(b) (Continued)

	Definition of test positivity: reported using analyser device (included in main analysis for review), and by naked eye inspection alone Blinding reported: not stated Timing of samples: not reported; on presentation
Target condition and reference standard(s)	Reference standard: RT-PCR; either Cobas 6800 (Roche) or the m2000 (Abbott) Definition of non-COVID cases: n/a Genetic target(s): E- and RDRP-gene (Roche) or E-gene and N-gene (Abbott) Samples used: NOP; specimen from the throat and nasal cavity up to the nasal bridge Timing of reference standard: as for index test Blinded to index test: not stated Incorporated index test: no
Flow and timing	Time interval between index and reference tests: paired All participants received same reference standard: yes; different assays Missing data: review team excluded 7 no longer PCR+ve at time of home visit (1 asymptomatic, 6 symptomatic) - Veritor rapid diagnostic (VRD) test result for 1 asymptomatic PCR – is given (VRD-) Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "the VRD (Ag) tests for this study were provided by the Dutch Ministry of Health, Welfare and Sport (VWS)" Publication status: preprint Source: medRxiv Author COI: "Jan Kluytmans is member of the National Outbreak Management Team of The Netherlands and of a committee which supports the implementation of the Corona-reporting App."

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		

Van der Moeren 2021(b) (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? No

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Van der Moeren 2021(b) *(Continued)*

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Veyrenche 2021
Study characteristics

Patient Sampling 2-group study estimating sensitivity and specificity:
 [1] PCR+ve hospital inpatients (n = 45)
 [2] pre-pandemic samples from "patients" (not otherwise specified) (n = 20)
 Recruitment: not stated; appears to be convenience as equal numbers per Ct value subgroup
 Prospective or retrospective: retrospective

Patient characteristics and setting Setting: inpatient
 Location: Montpellier University hospitals (Centre Hospitalier Universitaire de Montpellier, Montpellier)
 Country: France
 Dates: 14 March-11 April
 Symptoms and severity: 27/45, 60% cases "severe" according to WHO guideline (similar numbers per Ct subgroup)
 Demographics: median age:
 Ct ≤ 25, 66 (IQR 48-84)
 Ct 25-35, 63 (50-76)
 Ct ≥ 35, 58 (49-67)
 Controls 64 (35-93); 32/45, 71% male, all controls were male
 Exposure history: not stated

Index tests Test name: Coris COVID-19 Ag Respi-Strip
 Manufacturer: BioConcept, Gembloux, Belgium
 Antibody: NP
 Ag target: monoclonal ab
 Test method: CGIA
 Samples used: NP; collection not described
 Transport media: yes; "swabs were collected in various transport media (eSwab COPAN Amies 1 mL, Σ-Transwab liquid Amies, viral transport medium tube VTM-M 2.0mL)."
 Sample storage: unclear; RT-PCR conducted prospectively within a few hours but not reported for Ag testing

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Veyrenche 2021 (Continued)

	<p>Test operator: all tests were performed in the virology laboratory</p> <p>Definition of test positivity: visual, as per manufacturer IFU</p> <p>Blinding reported: not stated</p> <p>Timing of samples: day 1-20 pso, median Ct ≤ 25, 7 (4-10; presume this is IQR but could be range - is described as SD in paper) Ct 25-35, 8 (4-12) Ct ≥ 35, 11 (7-15)</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Allplex 2019-nCoV Assay (Seegene, Seoul, South Korea)</p> <p>Definition of non-COVID cases: pre-pandemic</p> <p>Genetic target(s): RdRp, N, E</p> <p>Samples used: NP; as for index</p> <p>Timing of reference standard: as for index</p> <p>Blinded to index test: yes, conducted first</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous; same swab</p> <p>All participants received same reference standard: no</p> <p>Missing data: none reported, no participant flow diagram reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "supported by Grants from Montpellier University Hospital and Montpellier University (MUSE)."</p> <p>Publication status: preprint</p> <p>Source: medRxiv</p> <p>Author COI: the authors declare that there are no conflicts of interest</p>

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 inclusions?	Unclear		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Veyrenche 2021 (Continued)

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 (Evaluations of single test application)	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)	
DOMAIN 3: Reference Standard	
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Reference standard does not incorporate result of index test?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk
Are there concerns that the target condition as defined by the reference standard does not match the question?	High
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes

Veyrenche 2021 (Continued)

Could the patient flow have introduced bias?

High risk

Villaverde 2021
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: paediatric patients aged 0-16 years attending EDs with symptoms compatible with SARS-CoV-2 infection and ≤ 5 days of evolution</p> <p>Recruitment: not stated; described as nested in a prospective, observational, multicenter cohort study</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 1620 (77)</p>
Patient characteristics and setting	<p>Setting: ED</p> <p>Location: one of 7 participating centres (Epidemiological Study of COVID-19 in Children of the Spanish Society of Pediatrics; EPICO-AEP)</p> <p>Country: Spain</p> <p>Dates: September and October 2020</p> <p>Symptoms and severity: all symptomatic; specific symptoms not reported</p> <p>Demographics: not reported</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Panbio</p> <p>Manufacturer: Abbott Rapid Diagnostic</p> <p>Antibody: nucleocapsid</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: NP; collected by trained nurses</p> <p>Transport media: none used</p> <p>Sample storage: none</p> <p>Test operator: attending paediatricians and nurse staff</p> <p>Definition of test positivity: visual line</p> <p>Blinding reported: yes, done first</p> <p>Timing of samples: all ≤ 5 days pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; not described</p> <p>Definition of non-COVID cases: single negative</p> <p>Genetic target(s): SARS-CoV-2 E and RdRp genes</p>

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Villaverde 2021 (Continued)

	Samples used: NP Timing of reference standard: performed within 24 h of specimen collection Blinded to index test: not stated Incorporated index test: not stated
Flow and timing	Time interval between index and reference tests: paired; simultaneous All participants received same reference standard: yes Missing data: none reported Uninterpretable results: none reported Indeterminate results (index test): none reported Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: "supported by a specific Research Grant of the Spanish Society of Pediatrics (Asociacion Espanola de Pediatra). This study was funded by project PI20/00095, from the Instituto de Salud Carlos III (Ministry of Economy, Industry and Competitiveness), and cofunded by the European Regional Development Funds. CDG is funded by the Spanish Ministry of Science and Innovation—Instituto de Salud Carlos III and Fondos FEDER (Contrato Rio Hortega CM19/00015)." Publication status: published Source: Journal of Pediatrics Author COI: the authors declare 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 inclusions?	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 (Evaluations of single test application)			

Villaverde 2021 (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)		
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	No	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
Reference standard does not incorporate result of index test?	Yes	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		High
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Did all participants receive a reference standard?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Weitzel 2020 [A]
Study characteristics

Patient Sampling	Single-group study to estimate sensitivity and specificity: samples from patients with respiratory symptoms and/or fever attending a private hospital ED
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Weitzel 2020 [A] (Continued)

Recruitment: convenience with deliberate sampling of positive cases to ensure a 2:1 distribution reported (5276 samples processed during study period)

Prospective or retrospective: retrospective

Number of samples (samples with confirmed SARS-CoV-2): 111 (80)

*17 samples included in [Porte 2020](#)

Patient characteristics and setting	<p>Setting: ED (private hospital)</p> <p>Location: Clínica Alemana de Santiago</p> <p>Country: Chile</p> <p>Dates: 16 March-26 April 2020</p> <p>Symptoms and severity: respiratory symptoms and/or fever; no further detail</p> <p>Demographics: median age 40 years; 50, 45% male (median age 38 years, 43% male for all samples tested during period)</p> <p>Exposure history: none reported</p>
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Index tests	<p>Weitzel 2020 [A] entry is for test [A] in the list below</p> <p>Test name:</p> <p>[A] Biocredit COVID-19 Ag One Step SARS-CoV-2 Antigen Test [B] COVID-19 Antigen Rapid Test Device StrongStep COVID-19 Antigen Test [C] Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit (Fluorescence immunochromatography) [D] Diagnostic Kit for 2019-Novel Coronavirus (2019-nCoV) Ag Test (Fluorescence Immunochromatographic Assay)</p> <p>Manufacturer:</p> <p>[A] RapiGEN Inc., Anyang-si, Gyeonggi-do, Republic of Korea [B] Liming Bio-Products Co., Jiangsu, China [C] Savant Biotechnology Co., Beijing, China [D] Bioeasy Biotechnology Co., Shenzhen, China</p> <p>Ag target: not reported in study</p> <p>Antibody: not reported in study</p> <p>Test method: [A] and [B] CGIA [C] and [D] FIA</p> <p>Samples used: NOP swabs in 3 mL UTM</p> <p>Transport media: UTM-RT System (Copan Diagnostics, Murrieta, CA, USA)</p> <p>Sample storage: stored at -80 °C; index tests applied on 28 and 29 April 2020</p> <p>Test operator: single, trained laboratory technician under BSL2 cabinet; visual outputs read by 2 independent observers with referral to 3rd if needed</p> <p>Definition of test positivity: as per manufacturer IFU; Beijing Savant test required use of manufacturer-supplied UV torch due to unavailability of reader device in Chile</p> <p>Blinding reported: yes; blinding stated</p> <p>Timing of samples: median 2 days (IQR 1-5 days); 88% (96/109) during the first week of symptoms</p>
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Weitzel 2020 [A] (Continued)

Target condition and reference standard(s)	Reference standard: RT-PCR; COVID-19 Genesig Real-Time PCR assay (Primerdesign Ltd., Chandler's Ford, UK). Ct ≤ 40 considered positive Definition of non-COVID cases: single PCR negative Genetic target(s): RdRp Samples used: NOP swabs; as for index Timing of reference standard: as for index test; median 2 days (IQR 1-5 days) Blinded to index test: yes; prior to index Incorporated index test: no
Flow and timing	Time interval between index and reference tests: same samples; index tests conducted after frozen storage All participants received same reference standard: yes Missing data: none reported; evaluation of Liming test was discontinued after initial poor performance (zero TP) Uninterpretable results: 2 tests had invalid results due to insufficient liquid migration (2 results excluded for each test) Indeterminate results (index test): visual interpretation of the Beijing Savant assay (using manufacturer-supplied UV torch) was reportedly difficult under daylight conditions; manufacturer's fluorescence reader not available in Chile Indeterminate results (reference standard): none reported Unit of analysis: participant
Comparative	
Notes	Funding: study authors report that the work received no funding; Savant Biotechnology Co. provided test kits free of charge Publication status: preprint Source: medRxiv Author COI: all authors declare 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?	No		
Was a case-control design avoided?	No		
Did the study avoid inappropriate inclusions?	Yes		

Weitzel 2020 [A] (Continued)

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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard?

Yes

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

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?

High

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?

No

Were the reference standard results interpreted without knowledge of the results of the index tests?

Yes

Reference standard does not incorporate result of index test?

Yes

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

High risk

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?

Yes

Did all patients receive the same reference standard?

Yes

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Weitzel 2020 [A] (Continued)

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Weitzel 2020 [B]
Study characteristics

Patient Sampling See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Patient characteristics and setting

Index tests [Weitzel 2020 \[B\]](#) entry is for test [B] in the list below; see [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries

Test name:

[A] Biocredit COVID-19 Ag One Step SARS-CoV-2 Antigen Test

[B] COVID-19 Antigen Rapid Test Device StrongStep COVID-19 Antigen Test

[C] Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit (Fluorescence immunochromatography)

[D] Diagnostic Kit for 2019-Novel Coronavirus (2019-nCoV) Ag Test (Fluorescence Immunochromatographic Assay)

Manufacturer:

[A] RapiGEN Inc., Anyang-si, Gyeonggi-do, Republic of Korea

[B] Liming Bio-Products Co., Jiangsu, China

[C] Savant Biotechnology Co., Beijing, China

[D] Bioeasy Biotechnology Co., Shenzhen, China

Ag target: not reported in study

Antibody: not reported in study

Test method: [A] and [B] CGIA
[C] and [D] FIA

Samples used: NOP swabs in 3 mL UTM

Transport media: UTM-RT System (Copan Diagnostics, Murrieta, CA, USA)

Sample storage: stored at -80 °C; index tests applied on 28 and 29 April 2020

Test operator: single, trained laboratory technician under BSL2 cabinet; visual outputs read by 2 independent observers with referral to 3rd if needed

Definition of test positivity: as per manufacturer IFU; Savant test required use of manufacturer-supplied UV torch due to unavailability of reader device in Chile

Blinding reported: yes; blinding stated

Timing of samples: median 2 days (IQR 1-5 days); 88% (96/109) during the first week of symptoms

Weitzel 2020 [B] (Continued)

Target condition and reference standard(s) See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Flow and timing See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Comparative

Notes

Weitzel 2020 [C]

Study characteristics

Patient Sampling See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Patient characteristics and setting See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Index tests [Weitzel 2020 \[C\]](#) entry is for test [C] in the list below; see [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Test name:

[A] Biocredit COVID-19 Ag One Step SARS-CoV-2 Antigen Test

[B] COVID-19 Antigen Rapid Test Device StrongStep COVID-19 Antigen Test

[C] Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit (Fluorescence immunochromatography)

[D] Diagnostic Kit for 2019-Novel Coronavirus (2019-nCoV) Ag Test (Fluorescence Immunochromatographic Assay)

Manufacturer:

[A] RapiGEN Inc., Anyang-si, Gyeonggi-do, Republic of Korea

[B] Liming Bio-Products Co., Jiangsu, China

[C] Savant Biotechnology Co., Beijing, China

[D] Bioeasy Biotechnology Co., Shenzhen, China

Ag target: not reported in study

Antibody: not reported in study

Test method: [A] and [B] CGIA

[C] and [D] FIA

Samples used: NOP swabs in 3 mL UTM

Transport media: UTM-RT System (Copan Diagnostics, Murrieta, CA, USA)

Sample storage: stored at -80 °C; index tests applied on 28 and 29 April 2020

Test operator: single, trained laboratory technician under BSL2 cabinet; visual outputs read by 2 independent observers with referral to 3rd if needed

Definition of test positivity: as per manufacturer IFU; Savant test required use of manufacturer-supplied UV torch due to unavailability of reader device in Chile

Blinding reported: yes; blinding stated

Weitzel 2020 [C] (Continued)

Timing of samples: median 2 days (IQR 1-5 days); 88% (96/109) during the first week of symptoms

Target condition and reference standard(s) See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Flow and timing See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Comparative

Notes

Weitzel 2020 [D]

Study characteristics

Patient Sampling See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Patient characteristics and setting See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Index tests [Weitzel 2020 \[D\]](#) entry is for test [D] in the list below; see [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Test name:

- [A] Biocredit COVID-19 Ag One Step SARS-CoV-2 Antigen Test
- [B] COVID-19 Antigen Rapid Test Device StrongStep COVID-19 Antigen Test
- [C] Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit (Fluorescence immunochromatography)
- [D] Diagnostic Kit for 2019-Novel Coronavirus (2019-nCoV) Ag Test (Fluorescence Immunochromatographic Assay)**

Manufacturer:

- [A] RapiGEN Inc., Anyang-si, Gyeonggi-do, Republic of Korea
- [B] Liming Bio-Products Co., Jiangsu, China
- [C] Savant Biotechnology Co., Beijing, China
- [D] Bioeasy Biotechnology Co., Shenzhen, China**

Ag target: not reported in study

Antibody: not reported in study

Test method: [A] and [B] CGIA
[C] and [D] FIA

Samples used: NOP swabs in 3 mL UTM

Transport media: UTM-RT System (Copan Diagnostics, Murrieta, CA, USA)

Sample storage: stored at -80 °C; index tests applied on 28 and 29 April 2020

Test operator: single, trained laboratory technician under BSL2 cabinet; visual outputs read by 2 independent observers with referral to 3rd if needed

Definition of test positivity: as per manufacturer IFU; Savant test required use of manufacturer-supplied UV torch due to unavailability of reader device in Chile

Blinding reported: yes; blinding stated

Weitzel 2020 [D] *(Continued)*

Timing of samples: median 2 days (IQR 1-5 days); 88% (96/109) during the first week of symptoms

Target condition and reference standard(s) See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Flow and timing See [Weitzel 2020 \[A\]](#) for full study details and QUADAS entries.

Comparative

Notes

Winkel 2020

Study characteristics

Patient Sampling Single-group study estimating sensitivity and specificity: football players, staff and referees from 13 professional football clubs and the national teams in the Netherlands; all tested approximately weekly by RT-PCR independent of presence of symptoms, 2 days prior to each match; results for symptomatic individuals were excluded

Recruitment: consecutive; all tested

Prospective or retrospective: prospective

Sample size (cases): 824 people provided 2425 samples; 52 positive on RT-PCR

Patient characteristics and setting Setting: screening (sports)

Location: professional football clubs and national football teams; author institutions included University Medical Center Utrecht, Royal Netherlands Football Association (KNVB)

Country: Netherlands

Dates: 1 October-9 November 2020

Symptoms and severity: all asymptomatic or pre-symptomatic. Of 68 PCR+ve results, 12 (18%) pre-symptomatic, 32 (47%) early infection (1st +ve in asymptomatic plus any subsequent +ves within 7 days), 21 (31%) late infection (≥ 7 days pso as long as symptoms had subsided or ≥ 7 days after 1st +ve PCR) 3 (4%) persistent viral shedding (> 4 weeks after 1st PCR+ve)

Demographics: median age 27 years (range 16-80 years, IQR: 21-40 years); 775, 94% male

Exposure history: not stated

Index tests Test name: Panbio COVID-19 Ag rapid test device

Manufacturer: Abbott (Lake Country, IL, USA)

Antibody: nucleocapsid

Ag target: not stated

Test method: CGIA

Samples used: NP

Transport media: none; swabs placed in lysis buffer

Sample storage: none; tested immediately

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Winkel 2020 (Continued)

Test operator: trained personnel (presume non-HCW)

Definition of test positivity: visual appearance of test line; weak unclear bands were considered inconclusive and were either excluded or considered positive or negative to determine best case and worst case scenarios

Blinding reported: yes; done first

Timing of samples: approximately weekly

Target condition and reference standard(s)

Reference standard: RT-qPCR; either Eurofins (Brugge, Belgium), Synlab Laboratories (Luik, Belgium), or U-diagnostics (Utrecht, the Netherlands).

Definition of non-COVID cases: Single negative

Genetic target(s): not stated

Samples used: seems to be combined NP+OP; "throat/nasopharyngeal swab"

Timing of reference standard: as for index

Blinded to index test: not stated

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: 96% paired swabs; 104 (4%) samples for PCR obtained on subsequent day

All participants received same reference standard: yes

Missing data: 1

Uninterpretable results: 1 invalid LFA excluded due to lack of control band

Indeterminate results (index test): 16 "inconclusive"; 5 in PCR+ve and 11 in PCR- (confirmed by subsequently negative PCR results)

Indeterminate results (reference standard): none reported

Unit of analysis: samples

Comparative

Notes

Funding: "this study was investigator-initiated and funded by the executing parties. No external funding was received. The Panbio COVID-19 Ag Rapid Tests were provided by the Ministry of Health, Welfare and Sport (VWS)"

Publication status: preprint

Source: medRxiv

Author COI: no COI statement was provided

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		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Winkel 2020 (Continued)

Did the study avoid inappropriate inclusions? 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 (Evaluations of single test application)
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? 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 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? No

Winkel 2020 (Continued)

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Yokota 2020(a)

Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity: PCR+ve cases obtained from symptomatic patients with COVID-19 were included</p> <ul style="list-style-type: none"> • (a) Yokota 2020(a) 17 NP swabs • (b) Yokota 2020(b) 17 saliva samples <p>(A further 307 negative saliva samples from asymptomatic people did not undergo Ag testing.)</p> <p>Recruitment: not reported</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 34 PCR+ve (17 NP, 17 saliva)</p>
Patient characteristics and setting	<p>Setting: laboratory-based; states samples from "Covid-19 patients"</p> <p>Location: unclear (author institution: Department of Hematology, Hokkaido University Faculty of Medicine, Sapporo, Japan)</p> <p>Country: Japan</p> <p>Dates: not reported</p> <p>Symptoms and severity: symptomatic; median 9 days (range, 2-14 days) pso</p> <p>Demographics: not reported</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Espline SARS-CoV-2</p> <p>Manufacturer: Fujirebio, Tokyo, Japan</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: immunochromatographic assay</p> <p>Samples used:</p> <ul style="list-style-type: none"> • (a) NP (collection not reported) • (b) saliva (collection not reported)

Yokota 2020(a) (Continued)

	<p>Transport media: not reported</p> <p>Sample storage: frozen samples; no further details</p> <p>Test operator: probably laboratory staff</p> <p>Definition of test positivity: yes; according to the manufacturer IFU</p> <p>Blinding reported: no; PCR performed before index test</p> <p>Timing of samples: median time of sampling was 9 days (range, 2-14 days) pso</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR Master Mixes (Thermo Fisher Scientific, Waltham, USA) and Real Time PCR System (Thermo Fisher Scientific). PCR tests were performed according to the manual by National Institute of Infectious Diseases (NIID, www.niid.go.jp/niid/images/epi/corona/2019-nCoVmanual20200217-en.pdf)</p> <p>RNA was extracted using QIAamp Viral RNA Mini Kit (QIAGEN, Hilden, Germany)</p> <p>Definition of non-COVID cases: N/A</p> <p>Genetic target(s): not reported</p> <p>Samples used:</p> <ul style="list-style-type: none"> • (a) NP • (b) saliva <p>Timing of reference standard: median time of sampling was 9 days (range, 2-14 days) after symptom onset</p> <p>Blinded to index test: yes; performed before index test</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: same samples</p> <p>All participants received same reference standard: yes</p> <p>Missing data: none reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported</p> <p>Unit of analysis: unclear</p>
Comparative	
Notes	<p>Funding: 'this study was supported by Health, Labour and Welfare Policy Research Grants 20HA2002.'</p> <p>Publication status: preprint</p> <p>Source: medRxiv</p> <p>Author COI: 'Espline SARS-CoV-2 and Lumipulse SARS-CoV-2 Ag kit were supplied by Fujirebio'. Authors declare no other competing interest</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Yokota 2020(a) *(Continued)*
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 inclusions? 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 (Evaluations of single test application)

Were the index test results interpreted without knowledge of the results of the reference standard? No

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

DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Yokota 2020(a) *(Continued)*

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Yokota 2020(b)
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity: PCR+ve cases obtained from symptomatic patients with COVID-19 were included</p> <ul style="list-style-type: none"> • (a) Yokota 2020(a) 17 NP swabs • (b) Yokota 2020(b) 17 saliva samples <p>(A further 307 negative saliva samples from asymptomatic people did not undergo Ag testing.)</p> <p>Recruitment: not reported</p> <p>Prospective or retrospective: retrospective</p> <p>Sample size (cases): 34 PCR+ve (17 NP, 17 saliva)</p>
Patient characteristics and setting	<p>Setting: laboratory-based; states samples from "Covid-19 patients"</p> <p>Location: unclear (author institution: Department of Hematology, Hokkaido University Faculty of Medicine, Sapporo, Japan)</p> <p>Country: Japan</p> <p>Dates: not reported</p> <p>Symptoms and severity: symptomatic; median 9 days (range, 2-14 days) pso</p> <p>Demographics: not reported</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: Espline SARS-CoV-2</p> <p>Manufacturer: Fujirebio, Tokyo, Japan</p> <p>Antibody: not reported</p> <p>Ag target: not reported</p> <p>Test method: immunochromatographic assay</p> <p>Samples used:</p>

Yokota 2020(b) (Continued)

- (a) NP (collection not reported)
- (b) saliva (collection not reported)

Transport media: not reported

Sample storage: frozen samples; no further details

Test operator: probably laboratory staff

Definition of test positivity: yes; according to the manufacturer IFU

Blinding reported: no; PCR performed before index test

Timing of samples: median time of sampling was 9 days (range, 2-14 days) pso

Target condition and reference standard(s)

Reference standard: RT-PCR Master Mixes (Thermo Fisher Scientific, Waltham, USA) and Real Time PCR System (Thermo Fisher Scientific). PCR tests were performed according to the manual by National Institute of Infectious Diseases (NIID, niid.go.jp/niid/images/epi/corona/2019-nCoVmanual20200217-en.pdf) RNA was extracted using QIAamp Viral RNA Mini Kit (QIAGEN, Hilden, Germany)

Definition of non-COVID cases: NA

Genetic target(s): not reported

Samples used:

- (a) NP
- (b) saliva

Timing of reference standard: median time of sampling was 9 days (range, 2-14 days) pso

Blinded to index test: yes; performed before index test

Incorporated index test: no

Flow and timing

Time interval between index and reference tests: same samples

All participants received same reference standard: yes

Missing data: none reported

Uninterpretable results: none reported

Indeterminate results (index test): none reported

Indeterminate results (reference standard): none reported

Unit of analysis: unclear

Comparative

Notes

Funding: "this study was supported by Health, Labour and Welfare Policy Research Grants 20HA2002."

Publication status: preprint

Source: medRxiv

Author COI: "Espline SARS-CoV-2 and Lumipulse SARS-CoV-2 Ag kit were supplied by Fujirebio". Authors declare no other competing interest.

Yokota 2020(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?	Unclear		
Was a case-control design avoided?	No		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Yokota 2020(b) *(Continued)*
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Did all participants receive a reference standard?	Yes
Could the patient flow have introduced bias?	Unclear risk

Young 2020
Study characteristics

Patient Sampling	<p>Single-group study to estimate sensitivity and specificity: patients with ≥ 1 symptoms of COVID-19 (within ≤ 7 days pso) at 21 study sites (n = 260) (2nd cohort of 361 samples from COVID suspects ≤ 5 days pso also evaluated to compare BD Veritor with Quidel Sofia 2 SARS Antigen FIA but excluded from review as only discrepant results on the 2 Ag assays underwent RT-PCR.)</p> <p>Recruitment: not stated</p> <p>Prospective or retrospective: prospective</p>
Patient characteristics and setting	<p>Setting: mixed; drive-through/tent (n = 42), outpatient clinic (n = 74), research clinic (n = 72), or skilled nursing facility (n = 66)</p> <p>Location: unclear; 21 geographically diverse study sites (author institutions BD Life Sciences, Louisiana State University Health Sciences Center, Tricore Reference Laboratory)</p> <p>Country: USA</p> <p>Dates: 5-11 June 2020</p> <p>Symptoms and severity: 110 (43%) cough, 98 (39%) muscle pain, 95 (37%) headache, 90 (35%) sore throat, 78 (31%) fever Of those at ≤ 6 d pso (n = 245): 94 (38%) with 1 symptom, 151 (62%) with ≥ 2 symptoms</p> <p>Demographics: median age 43 (range 18-90); 91 (36%) male</p> <p>Exposure history: not reported</p>
Index tests	<p>Test name: BD Veritor SARS-CoV-2 antigen test (no product codes)</p> <p>Manufacturer: Becton, Dickinson and Company, BD Life Sciences—Integrated Diagnostic Solutions, San Diego, CA</p> <p>Antibody: NP</p> <p>Ag target: not stated</p> <p>Test method: not stated; chromatographic immunoassay with analyser</p>

Young 2020 (Continued)

	<p>Samples used: nasal (presume AN); clinician collected from both nostrils (same swab); inserted approximately 2.5 cm up the nostril rolled 5 times along the mucosa</p> <p>Transport media: dry nasal swabs</p> <p>Sample storage: swabs were shipped for testing on dry ice (-70 °C);</p> <p>Test operator: not stated; Veritor testing was performed internally at BD (San Diego, CA, USA)</p> <p>Definition of test positivity: as per manufacturer IFU</p> <p>Blinding reported: yes; all personnel blinded to all other test results</p> <p>Timing of samples: all ≤ 7 d pso; median 3.0 d, mean 3.2 d. 38 (15%) 1 d pso, 57 (23%) 2 days, 54 (22%) 3 days, 40 (16%) 4 days, 37 (15%) 5 days, 19 (8%) 6 days, 6 (2%) 7 days</p>
Target condition and reference standard(s)	<p>Reference standard: Lyra SARS-CoV-2 PCR Assay (Quidel Corporation. Athens, OH); BD MAX real time SARS-CoV-2 PCR assay used for discordant testing</p> <p>Definition of non-COVID cases: as for cases (single negative)</p> <p>Genetic target(s): not stated</p> <p>Samples used: NP (n = 217) or OP (n = 34); clinician collected (if an NP swab was collected as part of standard care, the participant had the option of having an OP study swab taken in lieu of a second NP swab)</p> <p>Timing of reference standard: swabs taken prior to any study swabs (potential for contamination of nasal cavity)</p> <p>Blinded to index test: yes; performed at TriCore Reference Laboratories. "All testing was conducted with all personnel blinded to all other test results"</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: simultaneous (paired)</p> <p>All participants received same reference standard: yes</p> <p>Missing data: 9 excluded; 6 did not meet eligibility criteria and 3 had invalid specimens/results (2 on RT-PCR and 1 labelling error)</p> <p>Uninterpretable results: 3 invalid on at least 1 assay</p> <p>Indeterminate results (index test): none reported</p> <p>Indeterminate results (reference standard): none reported. Re-test of 9 'FN' results with BD MAX RT-PCR resulted in 2 confirmed FN (BD MAX+ve and sero+ve), 6 were BD Max-ve (incl 1 sero+ve) and 1 invalid (no result)</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: 'study was funded by Becton, Dickinson and Company; BD Life Sciences—Integrated Diagnostics Solutions. Non-BD employee authors received research funds as part of this work'</p> <p>Publication status: preprint</p> <p>Source: medRxiv</p>

Young 2020 (Continued)

Author COI: 'CRD, CF, KE, JCA, HR, and CKC are employees of Becton, Dickinson and Company; SY, None; CC, None; AM, None; CGF, None; CB, None; JA, None; RA, CEO and PI of Comprehensive Clinical Research LLC'

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 inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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?			High
DOMAIN 2: Index Test (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Young 2020 (Continued)

Reference standard does not incorporate result of index test? Yes

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

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

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

Did all participants receive a reference standard? Yes

Could the patient flow have introduced bias? High risk

Young 2021
Study characteristics

Patient Sampling Single-group study to estimate sensitivity and specificity: patients admitted to hospital for emergency care
 Recruitment: consecutive; all those who were admitted
 Prospective or retrospective: prospective
 Sample size (cases): 803 (214)

Patient characteristics and setting Setting: inpatient/emergency care
 Location: Oxford University Hospitals NHS Foundation Trust (Nuffield Department of Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK)
 Country: UK
 Dates: 23 December 2020-30 January 2021
 Symptoms and severity: 11 (8%) Ag positive had no COVID-related symptoms recorded (cough, dyspnoea, fever, ageusia or anosmia); 28/80 (35.0%) RDT- but PCR +ve had a pre-admission SARS-CoV-2 PCR+ve swab
 Demographics: not stated

Young 2021 (Continued)

	Exposure history: not stated
Index tests	<p>Test name: Innova</p> <p>Manufacturer: Innova Med Group, China (Xiamen Biotime Biotechnology)</p> <p>Antibody: N gene</p> <p>Ag target: not stated</p> <p>Test method: CGIA</p> <p>Samples used: "nose and throat" (collected by HCW)</p> <p>Transport media: none used</p> <p>Sample storage: none required; testing performed in the admitting department</p> <p>Test operator: "staff"; presume HCW</p> <p>Definition of test positivity: visual</p> <p>Blinding reported: yes</p> <p>Timing of samples: not stated; on admission</p>
Target condition and reference standard(s)	<p>Reference standard: RT-PCR; Thermo-Fisher Taq-Path</p> <p>Ct threshold not reported but range in Ct values was plotted; all < 35 Ct</p> <p>Definition of non-COVID cases: same as cases (single -ve PCR)</p> <p>Genetic target(s): not stated</p> <p>Samples used: same as for index test; transferred to the clinical laboratory in VTM</p> <p>Timing of reference standard: not stated</p> <p>Blinded to index test: unclear</p> <p>Incorporated index test: no</p>
Flow and timing	<p>Time interval between index and reference tests: paired swab; 732/803 swabs obtained on same day, 71/803 within 24 h of each other</p> <p>All participants received same reference standard: yes</p> <p>Missing data: yes; 18 invalid results reported</p> <p>Uninterpretable results: none reported</p> <p>Indeterminate results (index test): 2 invalid RDTs; 1 PCR+ve and 1 PCR-</p> <p>Indeterminate results (reference standard): 16 invalid on PCR; 1 RDT+ and 15 RDT-. The RDT+ sample was reported in the text as "indeterminate" on PCR, and the patient tested PCR+ve 5 days later</p> <p>Unit of analysis: participant</p>
Comparative	
Notes	<p>Funding: "one of the authors is an NIHR Clinical Lecturer and another is Robertson Foundation Fellow"</p> <p>Publication status: published as letter to the editor</p>

Young 2021 (Continued)

Source: Journal of Infection

Author COI: one of the authors declares lecture fees from Gilead outside the submitted work. No other authors have a conflict 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?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate inclusions?	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 (Evaluations of single test application)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	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 (Evaluations of serial (repeat) testing)			
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Reference standard does not incorporate result of index test?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	

Young 2021 (Continued)

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

High

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? No

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Yes

Did all participants receive a reference standard? No

Could the patient flow have introduced bias?

High risk

Ag: antigen; **ALP:** alkaline phosphatase; **AN:** anterior nasal; **BAL:** bronchoalveolar lavage; **CDC:** Centers for Disease Control; **CE:** conforms with European standards; **CGIA:** colloidal gold immunoassay; **CI:** confidence interval; **CLEIA:** chemiluminescent enzyme immunoassay; **COI:** conflict of interest; **Ct:** cycle threshold; **ED:** Emergency Department; **EUA:** emergency use authorization; **FIA:** fluorescence immunochromatographic; **FN:** false negative; **FP:** false positive; **GLY:** Glucose-Lactalbumin-Yeast; **GP:** general practitioner; **HCW:** healthcare worker; **ICU:** intensive care unit; **IFU:** instructions for use; **IPD:** individual patient data; **IQR:** interquartile range; **IVD:** in vitro diagnostic medical device; **LDT:** laboratory-developed test; **LFA:** lateral flow assay; **LFD:** lateral flow device; **LFT:** lateral flow test; **N/A:** not applicable; **NAAT:** nucleic acids amplification test; **NIH:** National Institutes of Health; **NHS:** National Health Service (UK); **NMT:** nasal mid-turbinate; **NOP:** naso-oropharyngeal; **NP:** nasopharyngeal; **OP:** oropharyngeal; **PCR:** polymerase chain reaction; **PHE:** Public Health England; **POC:** point of care; **PBS:** phosphate-buffered saline; **pso:** post-symptom onset; **QUADAS:** Quality Assessment tool for Diagnostic Accuracy Studies; **qPCR:** quantitative reverse transcription polymerase chain reaction; **RADT:** rapid antigen detection test; **RAT:** rapid antigen test; **RDT:** rapid diagnostic test; **RNA:** ribonucleic acid; **RDT:** rapid diagnostic test; **PCR:** reverse transcription polymerase chain reaction; **rPCR:** rapid reverse transcription polymerase chain reaction; **SD:** standard deviation; **TA:** tracheal aspirate; **TN:** true negative; **TP:** true positive; **UTM:** universal transport medium; **UV:** ultraviolet; **UW:** University of Washington; **VTM:** viral transport medium; **WHO:** World Health Organization

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Ahava 2021	Ineligible index test (lab-based antigen assay)
Aoki 2020	Ineligible index test (lab-based antigen assay)
Bello-Chavolla 2021	Ineligible index test (multiple assays used)
Chen 2021	Ineligible study design (proof of concept)
Corman 2020	Ineligible study design (analytical accuracy)
Cubas-Atienzar 2021	Ineligible study design (analytical accuracy)
Dalal 2021	Ineligible study design
Diao 2020	Exclude on index test - not commercially available

Study	Reason for exclusion
Dohla 2020	Ineligible index test
Downs 2021	Ineligible study design (multiple samples per participant; only gives overall positivity rates)
Eshghifar 2021	Inadequate sample size (also analytical accuracy)
Frnda 2021	Accuracy data cannot be extracted
Gili 2021	Ineligible index test (lab-based antigen assay)
Haage 2021a	Ineligible population
Haage 2021b	Ineligible study design
Herrera 2020	Ineligible reference standard
Hingrat 2020	Ineligible index test (lab-based antigen assay)
Hirotso 2020	Ineligible index test
Hirotso 2021	Ineligible index test (lab-based antigen assay)
Hledik 2020	Accuracy data cannot be extracted
Hoehl 2020	Ineligible study design
Kannian 2021	Ineligible population (cases PCR positive on NP and saliva; controls PCR negative on saliva but half positive on NP swabs)
Kashiwagi 2020	Inadequate sample size
Kobayashi 2021	Ineligible index test (lab-based antigen assay)
Koskinen 2021	Ineligible index test (lab-based antigen assay)
Kotsiou 2021	Accuracy data cannot be extracted (PPV only)
Kurstjens 2020	Ineligible index test
Kyosei 2020	Ineligible study design
Lefever 2021	Ineligible index test (laboratory-based assay)
Le Hingrat 2020	Ineligible index test
Li 2021	Ineligible index test (in-house microfluidic assay)
Liu 2021	Ineligible index test (in-house CLIA)
Mahari 2020	Ineligible study design
Mak 2020a	Ineligible study design (deliberate sampling by Ct values; analytical accuracy)
Mak 2020b	Ineligible study design (deliberate sampling by Ct values; analytical accuracy)

Study	Reason for exclusion
Marzinotto 2020	Accuracy data cannot be extracted
Mboumba 2021	Ineligible study design (analytical accuracy)
McAulay 2020	Ineligible index test (uses serum samples)
McDonald 2020	Ineligible reference standard
Menchinelli 2021	Ineligible index test (lab-based antigen assay)
Mohamed 2021	Ineligible study design
Moreno 2021	Accuracy data cannot be extracted
Nachtigall 2020	Ineligible index test
Ogawa 2020	Inadequate sample size
Pavelka 2020	Ineligible study design
Pekosz 2021	Ineligible reference standard (also reports subgroup of Young 2020)
Pellanda 2020	Ineligible index test
Peng 2020	Ineligible study design
Perchetti 2020	Ineligible study design
Pollock 2020a	Ineligible index test
Rastawicki 2021	Ineligible study design (serial testing in hospitalised patients)
Regev-Yochay 2021	Ineligible index test (multiple assays used)
Ren 2021	Ineligible index test (lab-based antigen assay)
Rodriguez-Manzano 2020	Ineligible index test
Rusanen 2020	Ineligible index test (lab-based antigen assay)
Scheiblaue 2021	Ineligible study design (analytical accuracy only)
Seitz 2021	Accuracy data cannot be extracted (confused reporting)
Seo 2020	Accuracy data cannot be extracted
Singh 2020a	Ineligible index test
Singh 2020b	Ineligible index test
Wang 2020	Ineligible index test (amplification-free nucleic acid immunoassay)
Wu 2020	Ineligible index test
Yamamoto 2021	Ineligible population (all COVID-19 inpatients; specificity in previously positive patients)

Study	Reason for exclusion
Yamayoshi 2020	Ineligible study design (analytical accuracy only)
Yokota 2021	Ineligible index test (lab-based antigen assay)
Yu 2020	Ineligible index test
Zamecnik 2020	Ineligible index test
Zeng 2020	Ineligible study design
Zhang 2020	Ineligible index test

Characteristics of studies awaiting classification [ordered by study ID]

Abdul-Mumin 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic Asymptomatic contacts Ghana Teaching hospital
Index tests	Standard Q SARS-CoV-2 Ag-RDT Sample: NP; on-site
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 193 (42)
Comparative	
Notes	

Abusrewil 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed Report se% by symptom status, by time pso and for Ct < 25 but no underlying numbers; needs author contact for subgroup data Tripoli, Libya Setting not reported; Biotechnology Research Center laboratories
Index tests	10 Ag-based rapid assays: Fluorecare, ESPLINE, RapiGen, Abbott Panbio, Flowflex, Acon, Assut Europe, Orient Gene, CerTest, Bioperfectus, AMP Sample: NP; on-site (different participants per assay)

Abusrewil 2021 *(Continued)*

Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 231 (108)
Comparative	
Notes	

Akashi 2021

Patient Sampling	Single-group (se only)
Patient characteristics and setting	Mixed Tsukuba, Japan Drive-through-type PCR centre
Index tests	QuickNavi-COVID19 Ag New digital version (not yet marketed) DK20-CoV-8M Sample: NP; on-site
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 96; 44 had new digital version
Comparative	
Notes	

Amer 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed; symptomatic, time pso Zagazig, Egypt University/medical centres; referred to the COVID-19 isolation unit
Index tests	SDQ Sample: NP + OP; after frozen storage
Target condition and reference standard(s)	RT-PCR Ct < 29, 29-36, 37-39
Flow and timing	Sample size (cases): 83 (69)
Comparative	
Notes	IPD is in Suppl 1

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Aranda-Diaz 2021

Patient Sampling	Single-group (se + sp; but does not meet minimum n cases)
Patient characteristics and setting	Primarily asymptomatic San Francisco, California, USA Residents and staff of congregate-living (homeless) shelters
Index tests	BinaxNOW Repeat/serial testing (not really accuracy) Sample: not reported; must be on-site
Target condition and reference standard(s)	RT-PCR but only in selected
Flow and timing	40 for accuracy; 828 eligible residents and 435 staff for uptake etc outcomes
Comparative	
Notes	Query inclusion, not really an accuracy study. Only first 40 had both RDT and PCR (all Ag-ve, 2 PCR +ve), then only some RDT+ had PCR

Baccani 2021

Patient Sampling	Unclear (single-group, but subgroup tested with LFAs)
Patient characteristics and setting	Inpatients, no further detail
Index tests	SDF, AFIAS LFA, and Lumipulse Sample: NP
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 201 (33) for Lumipulse; 93 (28) for SDF
Comparative	
Notes	

Bianco 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed; c66% asymptomatic; incl paediatric Italy; ED and occupational health wards
Index tests	LumiraDx Sample: nasal; direct

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Bianco 2021 *(Continued)*

Target condition and reference standard(s)	PCR, Xpert Xpress; NP
Flow and timing	Sample size (cases): 907 (298)
Comparative	
Notes	

Blairon 2021

Patient Sampling	Multi-group
Patient characteristics and setting	Not reported Belgium
Index tests	Bio-Rad, Novatec, LumiraDx Sample: respiratory
Target condition and reference standard(s)	PCR
Flow and timing	150+ve, 9-ve and 40 confounder panel
Comparative	
Notes	Probable exclude - samples pre-selected to represent certain Ct ranges

Bonde 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mainly asymptomatic Finland; hospital staff and patients with unknown SARS-CoV-2 status at paediatric department or ED
Index tests	BD Veritor Sample: OP; on-site
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 809 (29)
Comparative	
Notes	Multiple samples per participant (n = 674)

Boum 2021

Patient Sampling	
Patient characteristics and setting	
Index tests	
Target condition and reference standard(s)	
Flow and timing	
Comparative	
Notes	Details yet to be completed

Brihn 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mainly asymptomatic; both reported separately USA; all patients admitted through the ED
Index tests	Quidel Sofia Sample: AN; on-site
Target condition and reference standard(s)	PCR; NP
Flow and timing	Sample size (cases): 2039 (149)
Comparative	
Notes	

Bruins 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic Netherlands; HCW with mainly early symptoms
Index tests	Panbio Sample: NP; on-site
Target condition and reference standard(s)	TMA; NP + OP
Flow and timing	Sample size (cases): 1101 (84)
Comparative	
Notes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Bruzzoze 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Not reported Italy; lab-based retrospective
Index tests	Multiple (7 assays) Sample: respiratory; on-site
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 321 (253)
Comparative	
Notes	Sensitivity reported per assay, but underlying numbers not given. Would need author contact for inclusion

Caruana 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Asymptomatic Switzerland; ED patients
Index tests	SD Biosensor - Standard Q Sample: NP; on-site
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 116 (7)
Comparative	
Notes	

Cento 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed; data reported separately for subgroup with available symptom data Italy; patients presenting to ED with COVID symptoms or admitted to hospital for any other reason
Index tests	LumiraDx Sample: NP; on-site

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Cento 2021 *(Continued)*

Target condition and reference standard(s)	PCR; NP
Flow and timing	Sample size (cases): 960 (347)
Comparative	
Notes	

Chiu 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	2 cohorts 1) symptomatic, 2) asymptomatic outbreak screening 1) USA; 2) Hong Kong
Index tests	INDICAID, phase scientific Sample: nasal; on-site
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 1) 274 (75); 2) 22,994 (38)
Comparative	
Notes	

Christensen 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic USA; multiple sites
Index tests	BD Veritor triple test (COVID + Flu A+B) Sample: nasal
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 278 (60)
Comparative	
Notes	

Di Domenico 2021

Patient Sampling	Single-group (se + sp)
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Di Domenico 2021 (Continued)

Patient characteristics and setting	Asymptomatic Italy; healthy volunteers attending a Mediterranean fair
Index tests	Panbio and a new near patient ELISA Sample: 1) NP; 2) cyto-salivary
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 433 (36)
Comparative	
Notes	

Dierks 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Not reported Netherlands, HCWs
Index tests	LumiraDx; Nadal; TMA Sample: respiratory
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 444 (11); Nadal assay performed on only 215/444 samples
Comparative	
Notes	

Diez Flecha 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed; data reported separately for subgroup with available symptom data Spain; nursing home residents
Index tests	Panbio Sample: NP; on-site
Target condition and reference standard(s)	PCR; NP (obtained next day)
Flow and timing	Sample size (cases): 55 (36)
Comparative	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Diez Flecha 2021 *(Continued)*

Notes

Eleftheriou 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed; reported separately for symptomatic and asymptomatic Greece; paediatric inpatients
Index tests	Panbio Sample: NP
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 744 (51); 9 asymptomatic cases
Comparative	
Notes	

Fernandez 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed; reported separately for symptomatic and asymptomatic Spain; residential setting, symptomatic for COVID-19 or close contacts
Index tests	LumiraDx Sample: nasal
Target condition and reference standard(s)	PCR; NP
Flow and timing	Sample size (cases): 46 (24)
Comparative	
Notes	

Fernandez-Montero 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	se and sp reported separately for asymptomatic and higher-risk groups (close contact or mild symptoms). Also reported for Ct value < 20/25/30/35 Spain; asymptomatic adults from a semi-closed community
Index tests	Roche SARS CoV-2 Rapid Antigen test

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Fernandez-Montero 2021 *(Continued)*

Sample: NP, on-site

Target condition and reference standard(s)	RT-PCR < 20, 20 to < 25, 25 to < 30 and > 30
Flow and timing	Sample size (cases): 2543, (49)
Comparative	
Notes	

Ferte 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic, asymptomatic, risk situation, no risk situation Bordeaux University health campus screening facility
Index tests	Abbott Panbio Sample: NP
Target condition and reference standard(s)	RT-PCR, N gene, RdRp gene, N and RdRp gene, Ct < 23, < 30, < 33
Flow and timing	Sample size (cases): 692 (52)
Comparative	
Notes	

Fiedler 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed; not reported separately by symptom status Individuals tested by public health Essen-symptoms or asymptomatic contacts
Index tests	Liaison Sars CoV-2 Ag assay Sample: NP, Ag testing performed over 4 d in lab
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 182, 110 cases
Comparative	
Notes	Exclude: lab-based Ag testing performed

Ford 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic; asymptomatic; also reported by sex, race, age < or > 24, quarantine status Staff and students at University in Wisconsin
Index tests	Quidel Sofia SARS Antigen Fluorescent Immunoassay Sample: nasal swab
Target condition and reference standard(s)	RT-PCR < 25, > 25. Viral culture performed if discrepant PCR/Ag results. Subgenomic RNA testing if Ag or PCR pos
Flow and timing	Sample size (cases): 1058 (54)
Comparative	
Notes	Check overlap with Pray 2021 ; 10.15585/mmwr.mm695152a3

Frediani 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic; may need author contact for data by age/time USA: participants at rapid test centres aged ≥ 7 years, symptomatic for < 7 d
Index tests	Abbott BinaxNOW Sample: AN swabs; included staff-collected and self- or parent-collected swabs
Target condition and reference standard(s)	RT-PCR, Ct 0-25 subgroup
Flow and timing	Sample size (cases): 309 (93)
Comparative	
Notes	

Gitaka 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic and asymptomatic Kenya- HCWs and outpatients at Mary Help Hospital, students and general population at Mount Kenya University
Index tests	BD Veritor rapid Ag test Sample: AN for Ag, OP for PCR
Target condition and reference standard(s)	RT-PCR, Ct 0-25 subgroup

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Gitaka 2021 *(Continued)*

 Flow and timing Sample size (cases): 272 (47)

Comparative

Notes

Hagbom 2021

 Patient Sampling Single-group (se + sp)

 Patient characteristics and setting Hospitalised patients; asymptomatic HCWs. Median age and days pso reported
Sweden-hospital. Hospitalized patients and asymptomatic HCWs

 Index tests Rapid Response COVID-19 Antigen Rapid Test Cassette; DIAGNOS COVID-19 Antigen Saliva
Test; Panbio
Sample: saliva

 Target condition and reference standard(s) RT-PCR. All PCR pos samples were cultured

 Flow and timing Sample size (cases): 54 (15)

Comparative

Notes

Harmon 2021

 Patient Sampling Single-group (se + sp)

 Patient characteristics and setting Asymptomatic athlete screening programme

 Index tests Quidel Sofia-2 SARS- CoV-2 Antigen Tests at least 1 x per week

 Target condition and reference standard(s) PCR

 Flow and timing 23,462 weekly paired Ag/RT-PCR screening tests in 1931 athletes; 83 PCR+ve

Comparative

 Notes From Abstract: "Daily antigen testing was similar to RT- PCR testing two to three times a week in identifying infection. Antigen testing identified infection before the next scheduled PCR on 89 occasions and resulted in 234 days where potentially infectious athletes were isolated before they would have been isolated with RT- PCR testing alone"

Harris 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Asymptomatic community campus participants and critically unwell in hospital University of Arizona, staff and students
Index tests	Quidel Rapid Ag Test Sample: self-collected AN for Ag, NP for PCR
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 885 (305)
Comparative	
Notes	<ol style="list-style-type: none"> 1. Asymptomatic staff/students and critically unwell in ICU 2. Asymptomatic pos PCR followed for 1-2 weeks with Ct and Ag 3. 885 students and staff

Holzner 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic, asymptomatic; symptomatic with Ct < 30 Hospital in Germany, all presentations to ED
Index tests	Standard Q; Roche Sample: NP swab by HCW
Target condition and reference standard(s)	RT-PCR 0-20, 20-25, 25-30, > 30
Flow and timing	Sample size (cases): 2375 (551)
Comparative	
Notes	

Homza 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptoms vs asymptomatic Testing centre Czech Republic
Index tests	ECOTEST COVID-19 Ag rapid test STANDARD Q COVID-9 Ag ND COVID-19 Ag test

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Homza 2021 (Continued)

	JOYSBIO SARS-CoV-2 Ag rapid test kit
	Immupass Vivadiag SARS-COV-2 Ag rapid test
	Sample: NP. On site
Target condition and reference standard(s)	RT-PCR, < 20, 20-30, 30-40, viral culture used when Ag and PCR result differed
Flow and timing	Sample size (cases): 1141 (397)
Comparative	
Notes	

Homza 2021a

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic and asymptomatic, also categorised as PCR+ve and PCR pos+viable virus Testing centre Czech Republic
Index tests	ECOTEST COVID-19 Ag rapid test Sample: NP, on site
Target condition and reference standard(s)	RT-PCR, 0-19.9, 20-24.9, 24.9-30, 30-40. Viral culture used when Ag and PCR result differed.
Flow and timing	Sample size (cases): 494 (164)
Comparative	
Notes	

Kanji 2021

Patient Sampling	Single-group, Ag positive only
Patient characteristics and setting	Voluntary screening of asymptomatic HCWs
Index tests	Abbott Panbio or BD Veritor occurred on a weekly or twice-weekly basis
Target condition and reference standard(s)	Ag pos confirmed with RT-PCR
Flow and timing	71,847 Ag tests across 369 clinical sites
Comparative	
Notes	Probable exclude From Abstract: 87/71,847 Ag positive; 39 confirmed as TP on PCR

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kenyeres 2021

Patient Sampling	Single-group (sensitivity only)
Patient characteristics and setting	Suspected infection, no further subgroups Hospital Hungary, patients admitted with presumed SARS-CoV-2
Index tests	RapidGen - Biocredit Ag Sample: NP
Target condition and reference standard(s)	Positive by at least 2 PCRs
Flow and timing	Sample size (cases): 119 (65) pos by 2 PCR methods, 37 randomly selected for Ag
Comparative	
Notes	

Kim 2021

Patient Sampling	Single-group (se + sp) (2 study cohorts)
Patient characteristics and setting	1. 1. Symptomatic including days PSO, asymptomatic; Yeungnam University Medical Centre, South Korea. 2. 2. Symptomatic for days PSO; Indian Council of Medical Research (ICMR)-approved Rao's path lab
Index tests	GenBody COVAG025 Sample: NP swab
Target condition and reference standard(s)	RT-PCR, 1. se for Ct < 25 and 25-30
Flow and timing	Sample size (cases): 1. 130 (30); 2. 200 (100)
Comparative	
Notes	2 separate studies. 1 retrospective, 2 prospective

Kiro 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Patients with suspected infection, no further subgroups Tertiary care centre India
Index tests	STANDARD F COVID-19 Ag FIA test kit Sample: NP

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kiro 2021 (Continued)

Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 354 (136)
Comparative	
Notes	Ag result read by analyser

Kiyasu 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic, asymptomatic Japan, hospital screen for symptomatic/suspected infection
Index tests	QuickNavi-COVID19 Ag Sample: NP
Target condition and reference standard(s)	In-house and reference RT-PCR < 20, 20-24, 25-29, > 30
Flow and timing	Sample size (cases): 1934 (187)
Comparative	
Notes	

Klein 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic and asymptomatic. Symptom duration available for PCR+ve Drive in test centre Germany
Index tests	Panbio COVID-19 Ag rapid test Sample: 1. self-collected nasal 2. professional NP swab
Target condition and reference standard(s)	RT-PCR. Ct values and viral load reported for all PCR+ve samples
Flow and timing	Sample size (cases): 290 (45)
Comparative	
Notes	

Koелеman 2021

Patient Sampling	Single-group (se + sp); 2 study periods
Patient characteristics and setting	Symptomatic ED patients, nursing home patients, HCWs Teaching hospital, Netherlands
Index tests	Study period 1 Certest SARS-CoV-2 Roche SARS-CoV-2 Rapid Antigen Test Romed Coronavirus Ag Rapid Test BD Veritor SARS-CoV-2 point-of-care test Panbio COVID-19 Antigen rapid test Study period 2 Romed Coronavirus Ag Rapid Test Sample: NP- RT-PCR performed on day, 3 of 5 Ag tests were performed within 72 h, 2 Ag tests performed 1 month after collection
Target condition and reference standard(s)	RT-PCR; Ct < 20 and < 30
Flow and timing	Study period 1, 80 prospectively selected specimens, 40 PCR+ve Study period 2: 900 samples, 300 cases
Comparative	
Notes	2 different study periods

Kolwijck 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic HCWs Teaching hospital Netherlands
Index tests	Panbio COVID-19 Ag rapid test Sample: NP
Target condition and reference standard(s)	RT-PCR (NP + OP); <20, <25, <28, <30
Flow and timing	Sample size (cases): 443 (45)
Comparative	Implementation also reported but pos Ag not confirmed by PCR
Notes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Korenkov 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic; reported by days PSO Germany, routine SARS-CoV-2 testing centre
Index tests	Standard Q COVID-19 Ag Test (SD Biosensor/Roche) Sample: combined oro and NP swab
Target condition and reference standard(s)	RT-PCR <20, <25, <30, <35 +/-culture
Flow and timing	2028 tested by PCR, 118 samples also cultured. 210 cases PCR+ve
Comparative	
Notes	

Kritikos 2021

Patient Sampling	Single-group (sensitivity only)
Patient characteristics and setting	Hospitalized SARS CoV-2+ve patients Tertiary hospital, Switzerland
Index tests	One Step Immunoassay Exdia COVID-19 Ag (Precision Biosensor) and Standard Q COVID-19 Rapid Antigen Test (Roche) Sample: paired diluted NP and saliva samples, 1 undiluted NP swab
Target condition and reference standard(s)	RT-PCR
Flow and timing	58 confirmed SARS-CoV-2 patients
Comparative	
Notes	

Kumar 2021a

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Includes asymptomatic ED universal admission screen in tertiary private hospital India
Index tests	STANDARD Q COVID-19 Ag Sample: NP swab

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Kumar 2021a (Continued)

Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 288 (6 PCR+ve)
Comparative	
Notes	1 further case positive post-discharge (day 6 post-first neg PCR and Ag?). Query if 2x2 possible

Kumar 2021b

Patient Sampling	Single-group (se only)
Patient characteristics and setting	Asymptomatic pre-operative screen Tertiary eye care centre South India
Index tests	STANDARD Q rapid Ag test Sample: NP and throat
Target condition and reference standard(s)	RT-PCR, Ct < 40 positive
Flow and timing	Sample size (cases): 204 (12)
Comparative	
Notes	

Kurihara 2021

Patient Sampling	Single group (se + sp)
Patient characteristics and setting	Includes asymptomatic Tsukuba Clinics, Ibaraki prefecture, Japan
Index tests	Quick Chaser Auto SARS-CoV-2 Mizuho Medy Sample: NP; immediately
Target condition and reference standard(s)	RT-PCR Ct < 20, 20-24, 25-29, ≥ 30
Flow and timing	Sample size (cases): 1401 (83)
Comparative	
Notes	

Kweon 2021

Patient Sampling	Single group (se + sp) 2 groups combined n = 38 symptomatic patients (200 specimens) But also a 2nd group 'non-COVID' n = 122 specimens few details on same
Patient characteristics and setting	Symptomatic (serial testing) Second asymptomatic group Time from onset < 7, 8-14, > 14 d Chung-Ang University Hospital, Seoul
Index tests	AFIAS COVID-19 Ag Icroma COVID-19 Ag Sample: NP, after frozen storage
Target condition and reference standard(s)	RT-PCR Ct < 25, 25-30, 30-40
Flow and timing	38 patients in symptomatic group Symptomatic patients 38, specimens 200, pos specimens 141 'Non-COVID' group 122 specimens
Comparative	
Notes	DTA on symptomatic patients to which n = 122 COVID negative samples were added; check eligibility

Landaas 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Includes asymptomatic Symptoms ≤ 5 days, > 5 days Aker test station, Oslo, Norway
Index tests	Panbio Sample: NP and OP, on site
Target condition and reference standard(s)	RT-PCR Ct < 30, ≥ 30
Flow and timing	Sample size (cases): 3991 (250)
Comparative	
Notes	

Lee 2021

Patient Sampling	Single-group (se + sp) Retrospective selection known positives and presumably negatives
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Lee 2021 (Continued)

Patient characteristics and setting	No detail South Korea
Index tests	Standard Q Sample: NP, frozen storage
Target condition and reference standard(s)	RT-PCR Ct < 14.9, 15-19.9, 20-24.9, 25-29.9, 30-34.9, ≥ 35
Flow and timing	Sample size (cases): 680 (83)
Comparative	
Notes	Samples retrospectively selected i.e. 380 known positives selected based on calculated Ct value distribution for population; query eligibility

Le Goff 2021

Patient Sampling	Single group (se + sp)
Patient characteristics and setting	Includes asymptomatic COVISAN test centres, Paris, France
Index tests	Standard Q Sample: NP and also saliva on-site
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 1718 (117)
Comparative	
Notes	LAMP also compared

Leixner 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic Days 0-3, 0-5 ED, Klinik Landstrasse, Vienna, Austria
Index tests	AMP RAT Ameda Sample: NP, on site NP + OP for PCR
Target condition and reference standard(s)	RT-PCR Ct < 25 Ct < 30

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Leixner 2021 *(Continued)*

Flow and timing	Sample size (cases): 392 (94)
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Comparative	
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Notes	
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Lindner 2021

Patient Sampling	Single subgroup (se + sp)
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Patient characteristics and setting	Symptomatic; presumably includes asymptomatic Ambulatory test facility, Berlin/Heidelberg, Germany
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Index tests	Espline, Sure Status, Mologic Sample: NP + OP
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Target condition and reference standard(s)	RT-PCR B.1.1.7
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Flow and timing	Sample size (cases): 1692 (whole group) Cases = 354, cases B.1.1.7 220
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Comparative	
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Notes	Appears this is a B.1.1.7 subgroup analysis of a larger DTA study
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Lv 2021

Patient Sampling	Single-group (se only)
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Patient characteristics and setting	Confirmed COVID-19 patients; both antibody positive and negative Shanghai Public Health Clinical Center
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Index tests	Diagnostic Kit for COVID-19 Antigen Test (Colloidal Gold) (Kehua Bio-engineering, China) Sample: NP
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Target condition and reference standard(s)	RT-PCR NP swab
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Flow and timing	Sample size (cases): 85 (85)
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Comparative	
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Notes	
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Mack 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Includes asymptomatic USA, Surveillance NFL players and staff
Index tests	Quidel Sofia Repeat/serial testing Sample: NP, Ag available within 1 h (presume on site)
Target condition and reference standard(s)	RT-PCR but also more complex definition of a case see Fig 1 algorithm
Flow and timing	10,982 samples; PCR+ve cases = 174, adjudicated+ve cases = 130
Comparative	May not give DTA
Notes	

Matsuda 2021

Patient Sampling	Single-group (se + sp) for each Ag test
Patient characteristics and setting	Symptomatic < 10 days Slightly contradictory r/e asymptomatic cases Sao Paulo, Brazil 3 service outpatient/inpatient/private clinics/hospitals in Sao Paulo Met
Index tests	ECO Test ECO Diagnostica Panbio Sample: NP, Ag POC presumably (15 min)
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 108 (31)
Comparative	
Notes	

McKay 2021

Patient Sampling	Single-group (se + sp); separate groups per RAT
Patient characteristics and setting	Includes asymptomatic Nursing home, Georgia, USA
Index tests	Repeat/serial testing x3 rounds BinaxNow

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

McKay 2021 (Continued)

 Sample: AN, for all Ag tests
 NP for RT-PCR first round of testing

Target condition and reference standard(s)	RT-PCR Ct < 30, Ct ≥ 30
Flow and timing	Sample size (cases): 532 (PCR-confirmed cases = 105, PCR+ve and/or Ag+ve = 113: 21/101 samples pos by PCR and/or Ag were culture-positive)
Comparative	
Notes	

Muhi 2021

Patient Sampling	Single-group (sp), designed as se + sp but no cases identified
Patient characteristics and setting	Includes asymptomatic 3 x hospitals, Melbourne, Australia
Index tests	Panbio Sample: deep nasal+OP
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 2413 (0)
Comparative	
Notes	

Nordgren 2021

Patient Sampling	Single-group (se + sp); separate groups per RAT
Patient characteristics and setting	Symptomatic Östergötland, Sweden
Index tests	Panbio, Zhejang Orient gene Sample: NP, stored at 4 °C RAT tested within 7/7
Target condition and reference standard(s)	RT-qPCR (but don't see viral loads?) Ct < 20, 20-25, 25-30, > 30 Viral culture Seasonal CoV
Flow and timing	Sample size (cases): Panbio 286 (PCR+ve cases =156); Orient Gene 332 (PCR+ve cases =156)
Comparative	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Nordgren 2021 (Continued)

Notes

Norizuki 2021

Patient Sampling	Single-group (se only)
Patient characteristics and setting	Includes asymptomatic Airport quarantine, Japan
Index tests	Repeat/serial testing ESPLINE Sample: NPS x 2, Swab Anterior Nasal, Swab Anterior tongue, Saliva x 2
Target condition and reference standard(s)	RT-qPCR Viral load $\geq 10^4$, $< 10^4$
Flow and timing	Sample size (cases): 20 (20) 97 person day samples
Comparative	
Notes	Also lab based quantitative Aqs, Lumipulse and LAMP

Oh 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Includes asymptomatic Hospitalized & ED presentations in Seoul
Index tests	Repeat/serial testing (some cases) Standard Q Sample: NPS, on site
Target condition and reference standard(s)	RT-PCR Ct ≤ 30 , ≤ 25
Flow and timing	118 paired tests from 98 patients Cases = 40
Comparative	
Notes	

Orsi 2021

Patient Sampling	Single-group (se + sp)
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Orsi 2021 (Continued)

Patient characteristics and setting	Symptomatic Symptoms < 7, 7-14 days ED, San Martino, Genoa, Italy
Index tests	FREND COVID-19 As assay Standard F Sample: NPS Tested in lab within 8 h
Target condition and reference standard(s)	RT-PCR Ct < 26, 26-30, 31-35
Flow and timing	Sample size (cases): 110 (60)
Comparative	
Notes	

Osmanodja 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Includes asymptomatic Ambulatory test facilities, Charité, Berlin
Index tests	Dräger On site Sample: self-collected AN swabs Ag NP/OP - PCR
Target condition and reference standard(s)	RT-PCR Viral load (RNA copies): < 1 million, 1-10 million, > 10 million Variant B.1.1.7 or WT
Flow and timing	Sample size (cases): 379 (70)
Comparative	
Notes	

Perez-Garcia 2021

Patient Sampling	Two groups (se + sp)
Patient characteristics and setting	Mixed (84% symptomatic) Reports se by time pso Spain Setting not reported; Servicio de Microbiología Clínica, Hospital Universitario Príncipe de Asturias, Madrid

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Perez-Garcia 2021 *(Continued)*

Index tests	Panbio, STANDARD F (SD Biosensor, Inc.) Sample: NP in 3 mL of UTM, lab
Target condition and reference standard(s)	RT-PCR by Ct ≤ 20, Ct = 20–25, Ct= 25-30, Ct > 30
Flow and timing	Sample size (cases): 356 (170) and 186 control
Comparative	
Notes	

Qahtani 2021

Patient Sampling	Single-group; designed as se + sp, zero cases identified
Patient characteristics and setting	Mainly asymptomatic, passengers at airport Canada Vancouver International Airport
Index tests	Panbio (Abbott) Sample: NP, on-site
Target condition and reference standard(s)	PCR
Flow and timing	Sample size (cases): 592 (0)
Comparative	
Notes	

Revollo 2021

Patient Sampling	Single-group (se)
Patient characteristics and setting	Not reported; those negative on Ag tests before 12 h of event were included Reports result at day 1 (baseline) and day 8 (follow-up assessment) Spain A mass-gathering indoor event (a live concert), Sala Apolo, Barcelona
Index tests	Panbio (Abbott) Sample: NP, on-site
Target condition and reference standard(s)	Transcription-mediated amplification test (TMA, Procleix Panther, Grifols) and RT-PCR; cell culture
Flow and timing	Sample size (cases): 960 (28 cases with TMA, 2 cases with RT-PCR)
Comparative	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Revollo 2021 (Continued)

Notes

Reza 2021

Patient Sampling	Single-group (se)
Patient characteristics and setting	Mixed cases and contacts Belgium Setting not reported; Department of Laboratory Medicine, Service of Medical Microbiology, Yvoir
Index tests	Biospeedia COVID-19 speed-Antigen Test and Abbott Panbio Sample: NP, samples collected in UTM tubes, lab
Target condition and reference standard(s)	RT-PCR Results by high (Ct < 25), moderate (Ct ≥ 25 and < 30) and low (Ct ≥ 30) viral load groups
Flow and timing	Sample size (cases): 401 (232)
Comparative	
Notes	

Seynaeve 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed (76% symptomatic) Belgium Patients admitted to the ED and from the testing centre of the CHU Liège
Index tests	COVID-19 Ag Respi-Strip kit (Coris Bioconcept) and the coronavirus Ag rapid test cassette from Healgen Scientific, LLC Sample: NP, PB saline solution and lab-based
Target condition and reference standard(s)	RT-PCR Results by Ct 16.7-37.3 and Ct ≤ 31.00
Flow and timing	Sample size (cases): 63 convenience sample (48) 100 random sample (50)
Comparative	
Notes	

Shah 2021

Patient Sampling	Single-group (se + sp)
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Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Shah 2021 (Continued)

Patient characteristics and setting	Mixed, symptomatic and asymptomatic ≤ 7 d pso USA Unvaccinated registrants, community testing site in Oshkosh, Wisconsin
Index tests	Abbott's BinaxNOW Sample: AN, supervised and self-collected
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 2086 (315)
Comparative	
Notes	

Shaikh 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic children < 20 years (symptoms < 7 d) < 7 years and 7–20 years USA Primary care practice
Index tests	Abbott BinaxNOW Sample: Nasal (mid turbinate)
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 199 (39)
Comparative	
Notes	

Smith 2021a

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Mixed, symptomatic and asymptomatic ≤ 7 d pso USA, ED of community hospitals in Maryland
Index tests	Sofia SARS rapid Ag FIA (Sofia analysers used) Sample: NP, by trained staff

Smith 2021a (Continued)

Target condition and reference standard(s)	RT-PCR Results by Ct values
Flow and timing	Sample size (cases): 2887 (235)
Comparative	Ag testing in the laboratory; turn around time 1.2 h
Notes	

Smits 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic (emergency) GP Netherlands
Index tests	Panbio Sample: NP
Target condition and reference standard(s)	RT-PCR; ct < 45, ct < 32
Flow and timing	Sample size (cases): 534 (70)
Comparative	
Notes	

Sood 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Asymptomatic and symptomatic children USA; walk-up community-based COVID-19 testing site, Los Angeles
Index tests	BinaxNOW Sample: AN; collected by trained study staff
Target condition and reference standard(s)	RT-PCR Oral fluid specimens for RT-PCR were self-collected by participants and observed by trained staff Results by Ct ≤ 25; Ct 25.1-30; Ct > 30
Flow and timing	Sample size (cases): 774 (226)
Comparative	
Notes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Sterbenc 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Includes asymptomatic Slovenia HCW working at the University Clinic of Respiratory and allergic disease
Index tests	SARS-CoV-2 rapid Ag test; repeat testing (Roche Diagnostics GmbH, Mannheim, Germany) Sample: NP, collected into UTM
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 36; 191 swabs over 6 testing days (2)
Comparative	
Notes	

Suliman 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Asymptomatic (88%) and mildly symptomatic USA; free community testing sites in Holyoke, Massachusetts
Index tests	Access Bio CareStart COVID-19 RDT (CareStart) Sample: AN, collected by trained personnel
Target condition and reference standard(s)	RT-PCR By Ct \geq 30 and Ct < 30
Flow and timing	666 tests (from 591 participants) - results by sample tested; 52 positive samples
Comparative	
Notes	

Terpos 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic; patients reporting symptoms for a maximum of 7 d were included Slovenia, Primary Care Health Care institution and General Hospital Jesenice
Index tests	COVID-19 Ag detection kit (colloidal gold), Zhuhai Lituo Biotechnology, China; Includes comparison by sample site

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Terpos 2021 (Continued)

	Sample: NP, nasal
Target condition and reference standard(s)	RT-PCR By Ct < 25, Ct < 33, Ct < 40
Flow and timing	Sample size (cases): 358 NP (114); 358 nasal (109)
Comparative	
Notes	

Thakur 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Includes asymptomatic India, COVID-19-dedicated hospital (Delhi)
Index tests	PathoCatch/ACCUCARE, Lab Care Diagnostics Private Ltd., Sari Gam, India Sample: NP; onsite by a trained technician
Target condition and reference standard(s)	RT-PCR (NP + OP for RT-PCR) Results by Ct ≤ 25; Ct 25-29; Ct > 30
Flow and timing	Sample size (cases): 677 (84)
Comparative	
Notes	

Thell 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Symptomatic Results by days of symptom onset, type of care (ED vs PHC), type of symptom, gender and by age group Austria, ED and primary health care centres
Index tests	SARS-CoV-2 Rapid Antigen Test (Roche Diagnostics) Sample: swab type not specified; collected by experienced medical staff
Target condition and reference standard(s)	RT-PCR By Ct > 40, Ct > 30, Ct > 25, Ct > 20
Flow and timing	Sample size (cases): 541 (213)
Comparative	
Notes	

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Trobajo-Sanmartin 2021

Patient Sampling	Single-group (se + sp)
Patient characteristics and setting	Unclear Spain; setting unclear
Index tests	CerTest SARS-CoV-2 Card Test Sample: NP in UTM; stored at 4 °C for < 24 h until detection
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 240 (80)
Comparative	
Notes	Performed in the lab

Uwamino 2021

Patient Sampling	Cases only (72 RT-PCR+ve cases with 190+ve samples (se))
Patient characteristics and setting	Symptomatic By days of symptom onset Japan Hospital, single centre
Index tests	Espline SARS-CoV-2 RAD kit Includes comparison by sample site Sample: NP in UTM (collected by trained medical staff) Saliva (self-collected)
Target condition and reference standard(s)	RT-PCR; viral culture
Flow and timing	Sample size (cases): 190 samples (72) NP 117; saliva 73
Comparative	
Notes	Performed in the lab

Van Honacker 2021

Patient Sampling	Single-group (se + sp)- implementation part of the study
Patient characteristics and setting	Symptomatic, hospital admission Belgium

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Van Honacker 2021 *(Continued)*

	ED, Hospital
Index tests	SD Biosensor Sample: NP (Amies transport medium)
Target condition and reference standard(s)	RT-PCR (in house) By Ct values < 20, 20- < 26, 26- < 30, 30 to < 36 and > 36
Flow and timing	Sample size (cases): 4195 (369)
Comparative	
Notes	Performed in the lab Ag test on implementation part included; Ag tests on validation excluded

Wagenhäuser 2021

Patient Sampling	Single-group (se + sp)- implementation part of the study
Patient characteristics and setting	Any patient in the hospital; symptomatic and asymptomatic Results by symptom status not separated out for each test Germany; tertiary care hospital
Index tests	NADAL COVID-19 Ag Test Panbio MEDsan SARS-Cov-2 Antigen Rapid Test Sample: OP; by trained medical staff on site
Target condition and reference standard(s)	RT-PCR By viral load ≥ 10 (8) copies per mL, 10 (6-10 (8), 10 (4-10(6), < 10 (4)
Flow and timing	5056 samples, 101 positive samples
Comparative	
Notes	

Yin 2021

Patient Sampling	Single-group (se + sp)- implementation part of the study
Patient characteristics and setting	Symptomatic outpatients Belgium; primary care or ED
Index tests	Panbio COVID-19 Ag Rapid Test Device, BD Veritor SARS-CoV-2, COVID-19 Ag Respi-Strip (Coris BioConcept, Belgium) and SARS-CoV-2 Rapid Antigen Test (SD Biosensor)

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

Yin 2021 (Continued)

	Sample: NP, onsite
Target condition and reference standard(s)	RT-PCR
Flow and timing	Sample size (cases): 494 (209)
Comparative	
Notes	

Young 2021a

Patient Sampling	Cluster-RCT: schools randomly assigned (1:1) to either a policy of offering contacts daily Ag testing over 7 d to allow continued school attendance (intervention group) or to follow usual policy of isolation of contacts for 10 d (control group)
Patient characteristics and setting	Asymptomatic student or staff contacts
Index tests	SARS-CoV-2 Ag LFD (Orient Gene, Huzhou, China)
Target condition and reference standard(s)	Routine SARS-CoV-2 PCR tests done outside of the study; dedicated study PCR testing in both study groups on day 2 and 7 of the testing or isolation period
Flow and timing	
Comparative	
Notes	

Ag: antigen; **AN:** anterior nasal; **Ct:** cycle threshold; **ED:** emergency department; **ELISA:** enzyme-linked immunosorbent assay; **HCW:** healthcare worker; **IPD:** individual patient data; **LFA:** lateral flow assay; **LFD:** lateral flow device; **NP:** nasopharyngeal; **OP:** oropharyngeal; **PCR:** polymerase chain reaction; **pso:** post-symptom onset; **RCT:** randomized controlled trial; **RDT:** rapid diagnostic test; **RT-PCR:** reverse-transcription polymerase chain reaction; **Se:** sensitivity; **sp:** specificity; **TMA:** transcription-mediated amplification

ADDITIONAL TABLES
Table 1. Description of studies

Participants		No. of studies (%)
Number of studies		152
Sample size (all studies)	Median (IQR)	326 (149, 744.5)
	Range	17, 5504
	Total	100462
Number of COVID-19 cases (all studies)	Median (IQR)	83.5 (45, 135)

Table 1. Description of studies (Continued)

	Range	0, 951
	Total	16822
Setting	COVID-19 test centre	67 (44.1)
	ED/Urgent care	11 (7.2)
	Hospital inpatient (* 1 includes outpatients)	12 (7.2)
	Hospital – any (including staff or patients)	9 (5.9)
	Laboratory-based	16 (10.5)
	Mixed	6 (4.0)
	School or university-based	6 (4.0)
	Screening (HCWs 2, general public 3)	5 (3.3)
	Shared living facility	4 (2.6)
	Quarantine centre	1 (0.7)
	Unclear	15 (9.9)
Symptom status	Symptomatic	55 (36.2)
	Mainly symptomatic	18 (11.8)
	Asymptomatic	13 (8.6)
	Mainly asymptomatic	4 (2.6)
	Mixed	41 (27.0)
	Not reported	21 (13.8)
Study design		
Recruitment structure	Single group – sensitivity and specificity	109 (71.7)
	Two or more groups - sensitivity and specificity	20 (13.2)
	Single group – sensitivity only	16 (10.5)
	Single group – specificity only	1 (0.7)
	Randomized trial	1 (0.7)
	Unclear	5 (3.3)
Reference standards		
Reference standard for COVID-19 cases	All PCR positive	150 (98.7)

Table 1. Description of studies (Continued)

	TMA	1 (0.7)
	Not applicable (controls only study)	1 (0.7)
Reference standard for non-COVID-19 cases		No. of studies = 136
	Single negative PCR	133 (97.8)
	Single negative TMA	1 (0.7)
	Pre-pandemic samples	2 (1.5)
Reference standard samples		
	Paired swabs (same sample site as index)	76 (50.0%)
	Paired swabs (alternative sample site to index)	26 (17.1)
	Same sample for both index and reference tests	49 (32.2)
	Unclear	1 (0.7)
Tests		No. of evaluations (%)
Total number of test evaluations		210
Number of tests per study	1	129 (84.9)
	2	7 (4.6)
	3	4 (2.6)
	4	8 (5.3)
	5	2 (1.3)
	6	1 (0.7)
	7	1 (0.7)
Assay format	CGIA	156 (74.3)
	FIA	20 (9.5)
	LFA (ALP)	10 (4.8)
	LFA (latex conjugated)	2 (1.0)
	LFA (not otherwise specified)	18 (8.6)
	Microfluidic FIA	4 (1.9)
Sample type	Includes NP (all participants)	141 (67.1)

Table 1. Description of studies (Continued)

	NP alone	118 (56.1)
	NP+OP	20 (9.5)
	NP or NP+OP	3 (1.4)
	Includes NP (some participants)	12 (5.7)
	NP or OP	9 (4.3)
	NP, OP or NP+OP	2 (1.0)
	NP or NMT	1 (0.5)
	Includes nasal	44 (20.9)
	Nasal+OP	19 (9.1)
	Nasal (AN)	13 (6.2)
	Nasal (NMT)	9 (4.3)
	Nasal (not otherwise specified)	3 (1.4)
	Other sample sites	10 (4.8)
	OP alone	3 (1.4)
	Saliva	3 (1.4)
	BAL or TW	3 (1.4)
	Buccal	1 (0.5)
	Sample site not specified	3 (1.4)
Sample testing	Direct testing	113 (53.8)
	VTM	60 (28.6)
	Saline	8 (3.8)
	VTM or other	3 (1.4)
	Direct or VTM	1 (0.5)
	Not specified	25 (12.0)
IFU compliance	No	81 (38.6)
	Yes	90 (42.9)
	Unclear	39 (18.6)
Sample collection	HCW	73 (34.8)

Table 1. Description of studies (Continued)

	Self-collected	16 (7.6)
	Trained 'personnel'	11 (5.2)
	Trained non-HCW	9 (4.3)
	Laboratory scientist	9 (4.3)
	Mixed	3 (1.4)
	Not specified	89 (42.4)
Sample testing	Laboratory scientist	66 (31.4)
	HCW	50 (23.8)
	Trained non-HCW	7 (3.3)
	Trained 'personnel'	2 (1.0)
	Self-tested	2 (1.0)
	Mixed (on-site)	2 (1.0)
	Not specified (laboratory-based)	47 (22.4)
	Not specified (on-site)	31 (14.8)
	Not specified (no details)	3 (1.4)

ALP: alkaline phosphatase; **AN:** anterior nasal; **BAL:** bronchoalveolar lavage; **CGIA:** colloidal gold immunoassay; **ED:** emergency department; **FIA:** fluorescent immunoassay; **HCW:** healthcare worker; **IQR:** inter-quartile range; **LFA:** lateral flow assay; **NMT:** nasal mid-turbinate; **NP:** nasopharyngeal; **OP:** oropharyngeal; **PCR:** reverse transcription polymerase chain reaction; **TMA:** transcription-mediated amplification; **TW:** throat wash; **VTM:** viral transport medium

Table 2. Summary of sensitivity and specificity results

Test	Evaluations; samples (cases)	Summary sensitivity % (95% CI)	Difference in sensitivity, (95% CI), P value	Summary speci- ficity % (95% CI)	Difference in specificity, (95% CI), P value
Primary analysis					
All studies reporting sensitivity and specificity	184; 117,372 (21,017)	69.3 (66.2to72.3)	-	99.3 (99.2to99.3)	-
All data for sensitivity (including 'sensitivity-only' evaluations)	209; 119843 (23,488)	68.9 (66.0to71.7)	-	-	-
All data for specificity (including 'specificity-only' cohort)	185; 117910 (21,017)	-	-	99.3 (99.2to99.3)	-

Table 2. Summary of sensitivity and specificity results (Continued)

Secondary analyses by symptom status					
Symptomatic	109; 50,574 (11,662)	73.0 (69.3 to 76.4)	Ref	99.1 (99.0 to 99.2) ^a	Ref
Asymptomatic	50; 40,956 (2641)	54.7 (47.7 to 61.6)	-18.2 (-26.1 to -10.4), <i>P</i> < 0.0001	99.5 (99.4 to 99.6)	0.4 (0.3 to 0.5)
Mixed symptoms or not reported	56; 19,359 (5344)	70.6 (64.8 to 75.8)	Comparison not done	99.4 (99.3 to 99.5)	Comparison not done
Restricted to studies including both symptomatic and asymptomatic participants					
Symptomatic	34; 13,757 (3243)	75.9 (69.7 to 81.2)	Ref	99.0 (98.8 to 99.2)	Ref
Asymptomatic	34; 25,827 (1666)	56.8 (48.5 to 64.7)	-19.2 (-29.1 to -9.2), <i>P</i> < 0.0001	99.5 (99.4 to 99.6)	0.5 (0.3 to 0.7)
Including data from 'sensitivity-only' evaluations					
Symptomatic	132; 52,939 (14,027)	72.4 (69.1 to 75.5)	Ref	-	-
Asymptomatic	56; 41,129 (2814)	49.4 (44.5 to 54.2)	-23.1 (-26.5 to -19.6), <i>P</i> < 0.0001	-	-
Mixed symptoms or not reported	63; 19,936 (5921)	70.6 (65.4 to 75.3)	Comparison not done	-	-
Subgroup analyses for symptomatic participants					
By setting for testing					
COVID-19 test centre	47; 23,602 (4369)	82.8 (80.2 to 85.2)	Ref	99.1 (99.0 to 99.2)	Ref
Hospital inpatient	20; 11,903 (2536)	51.6 (45.9 to 57.2)	-31.3 (-37.5 to -25.1), <i>P</i> < 0.0001	99.6 (99.4 to 99.7)	0.5 (0.3 to 0.7)
ED/urgent care	15; 5607 (1312)	70.9 (55.8 to 82.5)	-11.9 (-25.7 to 1.9), <i>P</i> = 0.090	99.2 (98.9 to 99.4)	0.1 (-0.2 to 0.497)
Laboratory-based	9; 4144 (2161)	57.2 (42.5 to 70.7)	-25.6 (-40.3 to -10.9), <i>P</i> = 0.001	98.7 (98.1 to 99.1)	-0.4 (-0.9 to 0.1)
Hospital - any	3; 1175 (418)	52.8 (37.7 to 67.5)	-30.0 (-45.6 to -14.4), <i>P</i> < 0.0001	97.8 (96.4 to 98.6)	-1.4 (-2.4 to -0.3), <i>P</i> = 0.013

Table 2. Summary of sensitivity and specificity results (Continued)

School/university	2; 374 (114)	67.1 (46.4 to 82.8)	-15.7 (-34.8 to 0.107)	97.7 (95.0 to 99.0)	-1.4 (-3.2 to 0.4), $P = 0.130$
Hospital in- or outpatient	1; 1384 (116)	66.4 (57.0 to 74.9)	-	98.8 (98.1 to 99.3)	-
Screening – HCW	1; 115 (24)	83.3 (62.6 to 95.3)	-	100 (96.0 to 100)	-
Shared living facility	1; 30 (20)	95.0 (75.1 to 99.9)	-	100 (69.2 to 100)	-
Setting not reported	5; 519 (204)	67.7 (41.7 to 86.0)	-	83.4 (36.0 to 97.8)	-
Mixed settings	5; 1721 (388)	80.7 (66.6 to 89.7)	-	98.3 (97.5 to 98.9)	-
By time after symptom onset					
Week 1	30; 15,323 (2408)	80.9 (76.9 to 84.4)	Ref	99.5 (99.3 to 99.6)	Ref
Week 2	13; 903 (224)	48.9 (37.9 to 60.1)	-32.0 (-43.9 to -20.1), $P < 0.0001$	99.3 (98.2 to 99.7)	-0.2 (-0.9 to 0.4), $P = 0.515$
Including data from ‘sensitivity-only’ evaluations					
Week 1 (sensitivity)	72; 18,555 (5640)	82.2 (79.2 to 85.0)	Ref	-	-
Week 2 (sensitivity)	40; 1798 (1119)	53.8 (48.0 to 59.6)	-28.4 (-32.6 to -24.2), $P < 0.0001$	-	-
Subgroup analyses for asymptomatic participants					
By eligibility for testing					
Testing widely available to any asymptomatic person	26; 31,904 (1758)	49.6 (42.1 to 57.1)	Ref	99.6 (99.5 to 99.7)	Ref
Testing of contacts or referred groups only	16; 7677 (703)	64.3 (54.6 to 73.0)	14.7 (2.7 to 0.016)	99.7 (99.5 to 99.8)	0.06 (-0.09 to 0.444)
No details about eligibility for testing	6; 242 (64)	44.5 (26.7 to 63.8)	-5.1 (-26.0 to 0.632)	85.4 (79.4 to 89.9)	-14.2 (-19.4 to -9.0), $P < 0.0001$
Including sensitivity-only cohorts					
Testing available to any asymptomatic person	26; 31,904 (1758)	49.5 (41.6 to 57.4)	Ref	-	-
Testing of contacts or referred groups only	21; 7815 (841)	61.7 (52.4 to 70.2)	12.2 (0.2 to 0.047)	-	-

Table 2. Summary of sensitivity and specificity results (Continued)

No details about eligibility for testing	7; 277 (99)	47.1 (30.1 to 64.8)	-2.4 (-22.2 to 0.811)	-	-
By study setting					
COVID-19 test centre	18; 19,253 (1195)	61.5 (54.0 to 68.4)	Ref	99.6 (99.5 to 99.7)	Ref
Screening – mass	7; 7776 (648)	45.1 (36.4 to 54.1)	-16.4 (-27.9 to -4.9), P = 0.005	99.4 (99.2 to 99.6)	-0.2 (-0.4 to -0.01), P = 0.042
School/university	5; 5174 (96)	47.9 (38.1 to 57.9)	-13.6 (-25.9 to -1.2), P = 0.031	99.6 (99.4 to 99.7)	-0.04 (-0.2 to 0.673)
Hospital inpatient	5; 2282 (105)	35.2 (26.7 to 44.8)	-26.2 (-37.9 to -14.6), P < 0.0001	100 (99.7 to 100)	0.3 (0.2 to 0.4)
ED/urgent care	2; 2547 (85)	95.1 (7.3 to 100)	33.6 (7.0 to 60.13)	99.6 (99.2 to 99.8)	-0.04 (-0.3 to 0.796)
Laboratory-based	2; 532 (131)	58.2 (21.8 to 87.4)	-3.3 (-43.1 to 36.5), P = 0.871	98.8 (97.0 to 99.5)	-0.9 (-2.0 to 0.1)
Hospital - any	1; 262 (90)	70.0 (59.4 to 79.2)		92.4 (87.4 to 95.9)	
Quarantine	1; 113 (47)	85.1 (71.7 to 93.8)	-	100 (94.6 to 100)	-
Screening – HCW	1; 2224 (128)	51.6 (42.6 to 60.5)	-	99.9 (99.6 to 100)	-
Screening – traveller	1; 145 (5)	40.0 (5.3 to 85.3)	-	100 (97.4 to 100)	-
Unclear	5; 284 (62)	47.8 (28.3 to 67.9)	-	77.8 (44.0 to 94.0)	-
Mixed ^a	2; 364 (49)	36.7 (23.4 to 51.7)	-	100 (98.8 to 100)	-
By time after confirmed contact					
Week 1	3; 1013 (110)	70.0 (60.8 to 77.8)	Ref	99.8 (99.1 to 99.9)	Ref
Week 2	3; 747 (61)	60.7 (48.0 to 72.0)	-9.3 (-24.3 to 5.6), P = 0.221	99.3 (98.3 to 99.7)	-0.5 (-1.2 to 0.2), P = 0.159
Additional subgroup and sensitivity analyses across all participants regardless of symptom status					
Sensitivity analysis by study design					
Restricted to single group	126; 93970 (14171)	70.8 (67.2 to 74.3)		99.4 (99.3 to 99.4)	
Subgroup analysis by sample type (based on all 228 evaluations; data here for studies reporting both sensitivity and specificity)					

Table 2. Summary of sensitivity and specificity results (Continued)

Includes NP (all participants)	128; 59,447 (13,270)	69.0 (65.3 to 72.4)	Ref	99.4 (99.3 to 99.4)	Ref
Nasal (all)	34; 33,128 (4032)	76.6 (70.3 to 81.9)	7.7 (0.9 to 14.5), $P = 0.027$	99.4 (99.3 to 99.4)	0.01 (-0.1 to 0.1), $P = 0.873$
Nasal + OP	10; 12654 (1407)	68.7 (55.1 to 79.6)	-0.3 (-13.2 to 12.7), $P =$	99.6 (99.5 to 99.7)	0.3 (0.1 to 0.4), $P < 0.0001$
Includes NP (some participants)	12; 7530 (1994)	71.8 (59.8 to 81.4)	2.9 (-8.6 to	98.4 (98.0 to 98.7)	-1.0 (-1.3 to -0.6), $P < 0.0001$
Saliva (all)	3; 837 (184)	20.5 (7.5 to 45.1)	-48.5 (-67.7 to -29.3), $P < 0.0001$	99.8 (98.9 to 100)	0.5 (0.2 to 0.8), $P =$
OP alone	2; 553 (214)	57.4 (26.6 to 83.4)	-11.5 (-43.8 to 20.7), $P = 0.484$	99.4 (97.7 to 99.9)	0.1 (-0.8 to 0.9), $P =$
Other	4; 849 (127)	55.4 (25.6 to 81.7)	-	83.7 (36.8 to 97.8)	-
Not specified	3; 4881 (304)	79.3 (68.7 to 86.9)	-	99.3 (99.0 to 99.5)	-
Direct comparisons by sample type					
NP alone	9; 2979 (682)	80.9 (70.5 to 88.3)	Ref	99.6 (99.2 to 99.8)	Ref
Nasal (any type)	9; 2710 (619)	78.1 (66.7 to 86.4)	-2.9 (-16.1 to 10.4), $P = 0.672$	99.6 (99.2 to 99.8)	0.0 (-0.4 to 0.3), $P =$
NP alone	6; 1134 (316)	56.7 (44.3 to 68.3)	Ref	99.5 (99.1 to 99.7)	Ref
Nasal (NMT)	6; 1133 (316)	64.4 (52.2 to 75.0)	7.8 (-9.1 to 24.6), $P = 0.367$	97.5 (96.7 to 98.0)	-2.0 (-2.7 to -1.3), $P < 0.001$
NP alone	4; 1963 (402)	58.5 (53.6 to 63.2)	Ref	99.9 (99.5 to 100)	Ref
Saliva	4; 1448 (305)	21.6 (17.4 to 26.6)	-36.8 (-43.5 to -30.1), $P < 0.0001$	99.9 (99.4 to 100)	0.0 (-0.2 to 0.2), $P =$
NP alone (including sensitivity only cohorts)	6; 2201 (640)	66.5 (53.0 to 77.8)	Ref		
Saliva (including sensitivity only cohorts)	6; 1589 (446)	17.1 (10.1 to 27.5)	-49.4 (-64.8 to -34.0), $P < 0.0001$		
Nasal (not otherwise specified) ^{b,c}	2; 1318 (264)	44.7 (38.6 to 50.9) ^a	-	100 (99.7 to 100) ^a	-

Table 2. Summary of sensitivity and specificity results (Continued)

Saliva ^{b,c}	2; 1221 (242)	23.1 (18.0 to 29.0) ^a	-	100 (99.6 to 100) ^a	-
Nasal (AN)	1; 132 (36)	86.1 (70.5 to 95.3)	-	100 (96.2 to 100)	-
Nasal (NMT)	1; 132 (36)	86.1 (70.5 to 95.3)	-	100 (96.2 to 100)	-
Sensitivity analysis for accuracy in children					
Children (studies reporting sensitivity and specificity)	10; 4652 (410)	62.7 (52.7 to 71.7)	-	99.4 (99.1 to 99.6)	-
Children (including sensitivity-only cohorts)	12; 4775 (533)	62.1 (53.4 to 70.1)	-	-	-
Children (including specificity-only cohorts)	12; 4766 (410)	-	-	99.4 (99.1 to 99.6)	-
<i>Restricted to studies including both age groups</i>					
Children	6; 1835 (264)	63.7 (48.0 to 76.9)	Ref	99.0 (98.4 to 99.4)	Ref
Adults	6; 10,007 (1047)	73.5 (61.1 to 83.1)	9.9 (-8.7 to 28.4), <i>P</i> = 0.297	99.7 (99.6 to 99.8)	0.7 (0.2 to 1.2), <i>P</i> = 0.007
Including sensitivity-only cohorts					
Children	7; 1839 (268)	60.1 (45.1 to 73.4)	Ref	-	-
Adults	7; 10,103 (1143)	70.8 (58.3 to 80.8)	10.8 (3.0 to 18.5), <i>P</i> = 0.006	-	-
Including specificity-only cohorts					
Children	9; 2517 (265)	-	-	99.0 (98.5 to 99.4)	Ref
Adults	9; 11,756 (1108)	-	-	99.7 (99.6 to 99.8)	0.7 (0.2 to 1.1), <i>P</i> =
Subgroup analyses by viral load					
Viral load in subgroups by Ct value^d					
Subgroup: < 20 Ct	26; 1108 (1108)	97.4 (95.0 to 98.6)	-	-	-
Subgroup: 20-25 Ct	27; 1384 (1384)	93.6 (90.0 to 96.0)	-	-	-
Subgroup: 25-30 Ct	48; 1724 (1724)	68.7 (61.6 to 75.0)	-	-	-
Subgroup: 25-33 Ct	22; 564 (564)	66.2 (55.8 to 75.1)	-	-	-
Subgroup: > 30 Ct	64; 2332 (2332)	18.7 (14.2 to 24.1)	-	-	-

Table 2. Summary of sensitivity and specificity results (Continued)

Subgroup: 30-35 Ct	8; 247 (247)	25.3 (12.2 to 45.3)	-	-	-
Subgroup: > 35 Ct	9; 142 (142)	5.6 (1.9 to 15.7)	-	-	-
Viral load in subgroups by RNA copy values					
Subgroup: $\geq 10^8$ RNA copies/mL	3; 80 (80)	95.0 (87.4 to 98.1)	-	-	-
Subgroup: $\geq 10^7$ RNA copies/mL	21; 608 (608)	98.4 (97.0 to 99.1)	-	-	-
Subgroup: $\geq 10^7$ to $< 10^8$ RNA copies/mL	3; 49 (49)	93.9 (82.7 to 98.0)	-	-	-
Subgroup: $\geq 10^6$ to $< 10^7$ RNA copies/mL	28; 597 (597)	94.0 (89.8 to 96.6)	-	-	-
Subgroup: $\geq 10^5$ to $< 10^6$ RNA copies/mL	31; 686 (686)	70.9 (57.4 to 81.5)	-	-	-
Subgroup: $\geq 10^4$ to $< 10^5$ RNA copies/mL	24; 582 (582)	36.7 (24.7 to 50.5)	-	-	-
Subgroup: $< 10^4$ RNA copies/mL	24; 825 (825)	7.5 (3.8 to 14.3)	-	-	-
Subgroup analysis by assay format					
CGIA	140; 95,926 (17,146)	68.5 (65.1 to 71.7)	Ref	99.4 (99.3 to 99.4)	Ref
FIA	19; 6987 (1507)	76.6 (68.2 to 83.4)	8.2 (-0.1 to 16.5), $P = 0.054$	97.5 (97.1 to 97.9)	-1.9 (-2.3 to -1.4), $P < 0.0001$
LFA (ALP)	7; 1645 (411)	61.4 (38.3 to 80.3)	-	99.8 (99.2 to 99.9)	-
LFA (latex-conjugated) ^c	2; 2048 (156)	81.3 (69.9 to 89.0)	-	100 (99.8 to 100)*	-
Microfluidic FIA	4; 1373 (343)	89.7 (63.0 to 97.8)	-	98.5 (97.6 to 99.1)	-
LFA (not otherwise specified)	12; 9393 (1454)	60.7 (45.0 to 74.4)	-	99.6 (99.4 to 99.7)	-

ALP: alkaline phosphatase; **AN:** anterior nasal; **CGIA:** colloidal gold immunoassay; **CI:** confidence interval; **ED:** emergency department; **FIA:** fluorescent immunoassay; **HCW:** healthcare worker; **LFA:** lateral flow assay; **NMT:** nasal midturbinate; **NP:** nasopharyngeal; **OP:** oropharyngeal

^aExcludes outlier with 8% specificity in 13 throat saliva or throat wash samples.

^b2x2 tables combined prior to calculating estimates.

^cSeparate pooling of sensitivity or specificity.

^dThe range in viral load associated with each group of cycle threshold (Ct) values is likely to vary considerably between study laboratories, for example, Ct 25-30 can vary in RNA copies by as much as $\sim 10^3$ /mL to $\sim 10^7$ /mL.

Table 3. Summary data by symptom status, test brand and compliance with manufacturer instructions for use

SYMPTOMATIC participants by test	All			IFU compliant		
	N evaluations; samples (cases)	Summary sensitivity % (95% CI)	Summary specificity % (95% CI)	N evaluations; samples (cases)	Summary sensitivity % (95% CI)	Summary specificity % (95% CI)
AAZ - COVID-VIRO	3; 1204 (534)	84.9 (61.5 to 95.2)	97.0 (95.4 to 98.1)	2; 572 (239)	91.3 (78.2 to 96.9)	94.0 (90.9 to 96.1)
Abbott - BinaxNOW COVID-19 Ag card	4; 2018 (358)	80.9 (67.6 to 89.6)	99.9 (99.5 to 100)	4; 2018 (358)	80.9 (67.6 to 89.6)	99.9 (99.5 to 100)
Abbott - Panbio COVID-19 Ag	24; 14,509 (3167)	74.8 (67.6 to 80.8)	99.7 (99.6 to 99.8)	11; 7718 (1397)	77.3 (68.7 to 84.0)	99.7 (99.5 to 99.8)
<i>Including sensitivity-only cohorts</i>	<i>32; 15,331 (3989)</i>	<i>74.2 (68.5 to 80.1)</i>	-	<i>16; 8339 (2018)</i>	<i>75.8 (68.8 to 81.7)</i>	-
Access Bio - CareStart COVID-19 Ag	1; 241 (69)	75.4 (63.5 to 84.9)	94.8 (90.3 to 97.6)	1; 241 (69)	75.4 (63.5 to 84.9)	94.8 (90.3 to 97.6)
Anhui Deepblue - COVID-19 Ag	1; 1205 (191)	47.1 (39.9 to 54.5)	100 (99.6 to 100)			
<i>Including sensitivity-only cohorts</i>	<i>2; 1382 (368)</i>	<i>60.7 (41.7 to 79.7)</i>	-			
Becton Dickinson - BD Veritor	5; 2498 (299)	73.9 (55.4 to 86.6)	99.1 (98.6 to 99.4)	1; 1384 (116)	66.4 (57.0 to 74.9)	98.8 (98.1 to 99.3)
<i>Including sensitivity-only cohorts</i>	<i>7; 2655 (456)</i>	<i>78.4 (63.8 to 88.2)</i>	-	<i>2; 1416 (148)</i>	<i>82.5 (52.5 to 95.3)</i>	-
BIONOTE - NowCheck COVID-19 Ag	2; 618 (181)	89.5 (84.1 to 93.2)	97.7 (95.8 to 98.8)	2; 618 (181)	89.5 (84.1 to 93.2)	97.7 (95.8 to 98.8)
BIONOTE - NowCheck COVID-19 Ag (Nasal)	1; 218 (79)	89.9 (81.0 to 95.5)	98.6 (94.9 to 99.8)	1; 139 (79)	89.9 (81.0 to 95.5)	98.6 (94.9 to 99.8)
Biosynex - Biosynex COVID-19 Ag BSS	1; 634 (297)	59.6 (53.8 to 65.2)	100 (98.9 to 100)			
Coris Bioconcept - COVID-19 Ag Respi-Strip	5; 1158 (585)	37.5 (28.4 to 47.7)	99.8 (98.8 to 100)	3; 765 (408)	34.3 (29.9 to 39.1) ^a	100 (99.0 to 100) ^{a,b}
Denka Co - QuickNavi COVID-19 Ag	2; 1633 (123)	84.2 (66.2 to 93.5) ^a	100 (99.8 to 100) ^{a,b}	2; 1633 (123)	84.2 (66.2 to 93.5) ^a	100 (99.8 to 100) ^{a,b}
DIALAB - DIAQUICK COVID-19 Ag	1; 99 (99)	61.6 (51.3 to 71.2)	-	1; 99 (99)	61.6 (51.3 to 71.2)	-
ECODiagnostica - COVID-19 Ag ECO	1; 150 (55)	69.1 (55.2 to 80.9)	97.9 (92.6 to 99.7)	1; 150 (55)	69.1 (55.2 to 80.9)	97.9 (92.6 to 99.7)

Table 3. Summary data by symptom status, test brand and compliance with manufacturer instructions for

use (Continued)						
Fortress Diagnostics - Coronavirus Ag	1; 1191 (191)	56.0 (48.7 to 63.2)	99.9 (99.4 to 100)			
Fujirebio - ESPLINE SARS-CoV-2	1; 129 (63)	39.7 (27.6 to 52.8)	97.0 (89.5 to 99.6)			
<i>Including sensitivity-only cohorts</i>	<i>4; 251 (185)</i>	<i>29.6 (14.6 to</i>	<i>-</i>			
Innova Medical Group - SARS-CoV-2 Ag	3; 3522 (830)	68.1 (47.2 to 83.6)	99.0 (98.5 to 99.3)	1; 1676 (372)	57.5 (52.3 to 62.6)	99.6 (99.1 to 99.9)
<i>Including sensitivity-only cohorts</i>	<i>5; 3943 (1251)</i>	<i>70.8 (58.1 to 80.9)</i>	<i>-</i>	<i>3; 2097 (793)</i>	<i>69.1 (58.3 to</i>	<i>-</i>
Joysbio Biotech - SARS-CoV-2 Ag	1; 265 (44)	70.5 (54.8 to 83.2)	99.1 (96.8 to 99.9)			
Lepu Medical - SARS-CoV-2 Ag Rapid Test	1; 100 (100)	54.0 (43.7 to 64.0)	-			
Liming Bio-Products - StrongStep COVID-19 Ag	1; 19 (9)	0 (0 to 33.6)	90.0 (55.5 to 99.7)			
LumiraDx - SARS-CoV-2 Ag	2; 741 (177)	91.2 (70.0 to 97.9)	98.6 (97.2 to 99.3)	2; 741 (177)	91.2 (70.0 to 97.9)	98.6 (97.2 to 99.3)
MEDsan GmbH - SARS-CoV-2 Ag	1; 184 (84)	45.2 (34.3 to 56.5)	97.0 (91.5 to 99.4)			
Mologic - COVID 19 Rapid Ag‡	1; 650 (192)	90.6 (85.6 to 94.3)	100 (99.2 to 100)	1; 650 (192)	90.6 (85.6 to 94.3)	100 (99.2 to 100)
Orient Gene/Healgen Scientific - Coronavirus Ag	1; 1189 (190)	48.9 (41.6 to 56.3)	100 (99.6 to 100)			
<i>Including sensitivity-only cohorts</i>	<i>2; 1284 (285)</i>	<i>67.2 (40.7 to</i>	<i>-</i>	<i>1; 95 (95)</i>	<i>82.1 (72.9 to</i>	<i>-</i>
Precision Biosensor - Exdia COVID-19 Ag	1; 293 (90)	52.2 (41.4 to 62.9)	99.0 (96.5 to 99.9)	1; 293 (90)	52.2 (41.4 to 62.9)	99.0 (96.5 to 99.9)
Quidel - SOFIA SARS Antigen FIA	4; 1064 (176)	80.0 (71.5 to 86.4)	99.4 (98.7 to 99.8)	3; 1000 (144)	76.4 (68.8 to 82.6)	99.5 (98.8 to 99.8)
RapiGEN - BIOCREDIT COVID-19 Ag	4; 714 (284)	61.5 (49.3 to 72.5)	98.4 (96.6 to 99.2)	2; 582 (195)	66.3 (52.9 to 77.5)	99.0 (97.3 to 99.6)
Savant Biotech - Huaketai SARS-CoV-2	1; 109 (78)	16.7 (9.2 to 26.8)	100 (88.8 to 100)			
SD Biosensor - Standard F COVID-19 Ag	4; 1742 (380)	74.3 (61.8 to 83.9)	97.4 (96.4 to 98.1)	2; 1129 (159)	75.5 (68.2 to 81.5)	97.2 (96.0 to 98.1)
<i>Including sensitivity-only cohorts</i>	<i>5; 1909 (547)</i>	<i>72.5 (63.2 to</i>	<i>-</i>	<i>3; 1296 (326)</i>	<i>72.1 (66.7 to</i>	<i>-</i>

Table 3. Summary data by symptom status, test brand and compliance with manufacturer instructions for

use (Continued)						
SD Biosensor/Roche - Standard Q COVID-Ag	26; 10,678 (2539)	78.6 (72.3 to 83.7)	98.7 (98.4 to 98.9)	15; 5116 (1197)	84.0 (79.2 to 87.9)	99.2 (98.8 to 99.4)
<i>Including sensitivity only cohorts</i>	<i>28; 10,798 (2659)</i>	<i>79.2 (72.9 to 84.3)</i>	-			
SD Biosensor - Standard Q COVID-Ag (Nasal)	4; 621 (189)	85.2 (79.4 to 89.6)	99.3 (97.9 to 99.8)	4; 621 (189)	85.2 (79.4 to 89.6)	99.3 (97.9 to 99.8)
Shenzhen Bioeasy Biotech - 2019-nCoV Ag	4; 1093 (202)	84.4 (72.4 to 91.7)	93.2 (91.3 to 94.6)	2; 855 (40)	72.5 (56.8 to 84.1)	92.5 (90.5 to 94.1)
Sichuan Mass Spectrometry Biotech - 2019-nCoV Ag	1; 85 (85)	22.4 (14.0 to 32.7)	-			
Siemens - CLINITEST Rapid COVID-19 Ag	2; 350 (163)	68.7 (48.0 to 83.8)†	100 (98.0 to 100) a,b	1; 178 (91)	80.2 (70.6 to 87.8)	100 (95.8 to 100)
Sugentech Inc - SGTI-flex COVID-19 Ag	1; 106 (78)	52.6 (40.9 to 64.0)	96.4 (81.7 to 99.9)	1; 106 (78)	52.6 (40.9 to 64.0)	96.4 (81.7 to 99.9)
SureScreen Diagnostics - SureScreen V	1; 1185 (189)	42.9 (35.7 to 50.2)	99.9 (99.4 to 100)			
ASYMPTOMATIC participants by test						
Abbott - BinaxNOW COVID-19 Ag card	6; 12,530 (588)	58.7 (45.6 to 70.6)	99.8 (99.7 to 99.8)	6; 12,530 (588)	58.7 (45.6 to 70.6)	99.8 (99.7 to 99.8)
Abbott - Panbio COVID-19 Ag	14; 4038 (561)	56.9 (42.8 to 69.9)	99.5 (99.1 to 99.7)	7; 2502 (279)	57.9 (35.4 to 77.5)	99.6 (99.3 to 99.8)
<i>Including sensitivity-only cohorts</i>	<i>17; 4138 (661)</i>	<i>57.8 (45.5 to 70.6)</i>	-	<i>8; 2557 (334)</i>	<i>55.4 (36.8 to 74.0)</i>	-
Access Bio - CareStart COVID-19 Ag	1; 1257 (165)	50.3 (42.4 to 58.2)	98.9 (98.1 to 99.4)	1; 1257 (165)	50.3 (42.4 to 58.2)	98.9 (98.1 to 99.4)
Becton Dickinson - BD Veritor	2; 2556 (203)	49.8 (32.1 to 67.5)	99.7 (99.3 to 99.8)			
BIONOTE - NowCheck COVID-19 Ag	1; 1326 (9)	55.6 (21.2 to 86.3)	100 (99.7 to 100)			
Coris Bioconcept - COVID-19 Ag Respi-Strip	1; 45 (14)	28.6 (8.4 to 58.1)	100 (88.8 to 100)	1; 45 (14)	28.6 (8.4 to 58.1)	100 (88.8 to 100)
Denka Co - QuickNavi COVID-19 Ag	1; 415 (33)	75.8 (57.7 to 88.9)	100 (99.0 to 100)	1; 415 (33)	75.8 (57.7 to 88.9)	100 (99.0 to 100)
Fujirebio - ESPLINE SARS-CoV-2	1; 15 (15)	13.3 (1.7 to 40.5)	-			
Innova Medical Group - SARS-CoV-2 Ag	2; 6224 (78)	38.5 (28.4 to 49.7)	100 (99.8 to 100)	1; 5504 (70)	40.0 (28.5 to 52.4)	99.9 (99.8 to 100)
Lepu Medical - SARS-CoV-2 Ag Rapid Test	1; 286 (101)	45.5 (35.6 to 55.8)	89.2 (83.8 to 93.3)			

Table 3. Summary data by symptom status, test brand and compliance with manufacturer instructions for use

Test brand	N (n)	Sensitivity (95% CI)	Specificity (95% CI)	N (n)	Sensitivity (95% CI)	Specificity (95% CI)
LumiraDX - SARS-CoV-2 Ag	1; 272 (9)	77.8 (40.0 to 97.2)	99.6 (97.9 to 100)	1; 272 (9)	77.8 (40.0 to 97.2)	99.6 (97.9 to 100)
Precision Biosensor - Exdia COVID-19 Ag	1; 239 (24)	33.3 (15.6 to 55.3)	100 (98.3 to 100)	1; 239 (24)	33.3 (15.6 to 55.3)	100 (98.3 to 100)
Quidel - SOFIA SARS Antigen FIA	1; 871 (17)	41.2 (18.4 to 67.1)	98.4 (97.3 to 99.1)	1; 871 (17)	41.2 (18.4 to 67.1)	98.4 (97.3 to 99.1)
RapiGEN - BIOCREDIT COVID-19 Ag	2; 140 (60)	63.2 (21.7 to 91.4)	98.8 (91.7 to 99.8)			
SD Biosensor - Standard F COVID-19 Ag	1; 55 (55)	43.6 (30.3 to 57.7)	-	1; 55 (55)	43.6 (30.3 to 57.7)	-
SD Biosensor/Roche - Standard Q COVID-Ag	12; 10,049 (551)	59.4 (49.6 to 68.5)	99.3 (99.1 to 99.4)	4; 5914 (250)	64.6 (51.3 to 75.9)	99.6 (99.4 to 99.7)
<i>Including sensitivity-only cohort</i>	<i>13; 10,052 (554)</i>	<i>60.4 (50.5 to 69.6)</i>	-			
Shenzhen Bioeasy Biotech - 2019-nCoV Ag	1; 44 (1)	0 (0 to 97.5)	79.1 (64.0 to 90.0)	1; 44 (1)	0 (0 to 97.5)	79.1 (64.0 to 90.0)
Siemens - CLINITEST Rapid COVID-19 Ag	2; 378 (126)	53.2 (44.5 to 61.7)	98.8 (96.4 to 99.6)	1; 92 (25)	60.0 (38.7 to 78.9)	100 (94.6 to 100)
SureScreen Diagnostics - SureScreen V	1; 286 (101)	28.7 (20.1 to 38.6)	97.8 (94.6 to 99.4)			

^aSeparate pooling of sensitivity or specificity.

^b2x2 tables combined prior to calculating estimates.

Table 4. Direct comparisons by test brand (any symptom status)

Test	N evaluations; samples (cases)	Summary sensitivity % (95% CI)	Difference in sensitivity, (95% CI), P value	Summary specificity % (95% CI)	Difference in specificity, (95% CI), P value
Panbio COVID-19 Ag (Abbott) vs Standard Q COVID-Ag (SD Biosensor/Roche); studies reporting both sensitivity and specificity					
Panbio	9; 3895 (1058)	56.7 (44.3, 68.3)	<i>Ref</i>	99.5 (99.1, 99.7)	<i>Ref</i>
Standard Q	9; 3301 (1055)	64.4 (52.2, 75.0)	7.8 (-9.1, 24.6), P = 0.367	97.5 (96.7, 98.0)	-2.0 (-2.7, -1.3), P < 0.001
Panbio COVID-19 Ag (Abbott) vs Standard Q COVID-Ag (SD Biosensor/Roche); summary sensitivity including 'sensitivity-only' cohort					
Panbio	10; 3977 (1140)	56.1 (45.0, 66.6)	<i>Ref</i>	-	-
Standard Q	10; 3372 (1126)	63.9 (53.0, 73.6)	7.8 (-7.3, 23.0), P = 0.311	-	-
Panbio COVID-19 Ag (Abbott) vs Coronavirus Ag (Orient Gene/Healgen Scientific); studies reporting both sensitivity and specificity					

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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Table 4. Direct comparisons by test brand (any symptom status) (Continued)

Panbio	2; 1968 (287)	60.7 (44.1, 75.2)	Ref	99.7 (99.3, 99.9)	Ref
Coronavirus Ag	2; 1377 (286)	63.3 (46.6, 77.3)	2.5 (-20.0, 25.1), $P = 0.825$	99.7 (99.2, 99.9)	0.02 (-0.38, 0.43), $P = 0.914$
Panbio COVID-19 Ag (Abbott) vs Coronavirus Ag (Orient Gene/Healgen Scientific); summary sensitivity including 'sensitivity-only' cohort					
Panbio	3; 2067 (386)	65.3 (50.0, 78.0)	Ref	-	-
Coronavirus Ag	3; 1472 (381)	70.3 (55.5, 81.8)	5.0 (-14.6, 24.6), $P = 0.617$	-	-
Standard Q COVID-Ag (SD Biosensor) Nasal kit vs NP kit					
Nasal kit	3; 489 (153)	85.0 (78.4, 89.8)	Ref	99.1 (97.3, 99.7)	Ref
NP kit	3; 489 (153)	83.0 (76.2, 88.2)	-2.0 (-10.2, 6.3), $P = 0.640$	99.4 (97.7, 99.9)	0.3 (-1.0, 1.6), $P = 0.653$

Table 5. Studies evaluating repeated (serial) antigen testing

Study	Population	Test and reference standard	Results
Kriemler 2021	<p>Pupils and teachers tested at primary or secondary school at T1 and or T2 (1 week apart). Schools were in high-incidence areas; children were required to be kept at home if they were sick beyond very mild symptoms such as runny nose or mild cough</p> <p>641 children and adolescents and 66 teachers tested at T1 and or T2; children provided 1170 samples (1 PCR+ve)</p>	<p>Index: SD Biosensor Standard Q; paired buccal swabs obtained by study staff and tested immediately on site</p> <p>Reference: single PCR (Seegene Allplex) targeting N, S, RdRP and E-gene; used paired buccal swabs</p>	<p>T1 (data included in single test application analysis)</p> <ul style="list-style-type: none"> • All participants <ul style="list-style-type: none"> ◦ Se 0% (95% CI 0.0% to 97.5%) (0/1) ◦ Sp 98.9% (95% CI 97.7% to 99.6%) (623/630) • Children <ul style="list-style-type: none"> ◦ Se 0% (95% CI 0.0% to 97.5%) (0/1) ◦ Sp 98.9% (95% CI 97.7% to 99.6%) (562/568) • Adults <ul style="list-style-type: none"> ◦ Se N/A (0 cases in adults) ◦ Sp 98.4% (95% CI 91.3% to 1.00%) (61/62) <p>T2</p> <ul style="list-style-type: none"> • All participants <ul style="list-style-type: none"> ◦ Se N/A (0 cases) ◦ Sp 99.5% (95% CI 98.7% to 99.9%) (656/659) • Children <ul style="list-style-type: none"> ◦ Se N/A (0 cases) ◦ Sp 99.7% (95% CI 98.8% to 100%) (600/602) • Adults <ul style="list-style-type: none"> ◦ Se N/A (0 cases) ◦ Sp 98.2% (95% CI 90.6% to 100%) (56/57) <p>The child with positive PCR at T1 was negative on both PCR and RDT at T2.</p> <p>4/9 positive RDTs were repeated immediately with the same buccal swab and remained positive.</p>

Table 5. Studies evaluating repeated (serial) antigen testing (Continued)

			9/9 positive RDTs were repeated at 2 h to 2 days using new buccal sample; all were negative both on RDT and PCR, respectively. All positive test lines categorized as weak to moderate
Love 2021	<p>PHE feasibility study of daily contact RDT testing for 7 days in place of self-isolation. Contacts of confirmed cases identified through NHS Test and Trace</p> <p>882/1760 (50.1%) contacts agreed to participate; 812/882 were sent a testing kit. In-study PCR results available for 346 contacts (64 PCR +ve)</p>	<p>Index test: Innova RDT; self-collected and self-tested nasal swabs</p> <p>Reference: subgroup provided samples for PCR (60% of those providing ≥ 1 RDT result, plus PCR results accessed for those having PCR outside of study); confirmatory PCR either if RDT+ve or at end of 7-day period</p>	<p>570/812 returned ≥ 1 RDT result (2946 samples in total)</p> <ul style="list-style-type: none"> • 102 with ≥ 1 positive RDT • 464 all negative RDTs • 4 negative or invalid RDTs <p>346/562 submitted swabs for PCR within the study protocol; se and sp of the RDT were</p> <ul style="list-style-type: none"> • Overall <ul style="list-style-type: none"> ◦ Se 82.8% (95% CI 71.3% to 91.1%) (53/64) ◦ Sp 99.3% (95% CI 97.5% to 99.9%) (280/282) • Symptomatic <ul style="list-style-type: none"> ◦ Se 88.9% (95% CI 75.9% to 96.3%) (40/45) ◦ Sp 80.0% (95% CI 44.4% to 97.5%) (8/10) • Asymptomatic <ul style="list-style-type: none"> ◦ Se 68.4% (95% CI 43.4% to 87.4%) (13/19) ◦ Sp 100% (95% CI 98.7% to 100%) (272/272) <p>Of the 11 RDT-negative/PCR+ve results, median Ct values were 24.0 (range 16.9-32.1) for ORF1ab gene and 25.5 (range 16.9-33.5) for E-gene; 6/11 self-reported symptoms.</p> <p>224/562 did not submit swabs for PCR, results obtained via NHS Test and Trace for 51/224</p> <ul style="list-style-type: none"> • Overall <ul style="list-style-type: none"> ◦ Se 84.2% (95% CI 60.4% to 96.6%) (16/19) ◦ Sp 100% (95% CI 89.1% to 100%) (32/32) <p>Secondary attack rates (i.e. transmission to contacts) reported for 160 contacts of 84 index cases: 10/160 confirmed PCR+ve, secondary attack rates 6.3% (95% CI 3.4% to 11.1%)</p> <p>Reported reasons for participation in study included: duty (298/882, 33.8%), assurance given from daily testing (268, 30.4%), escape from self-isolation restrictions (229, 26.0%)</p>
Smith 2021	<p>Daily testing of PCR +ve students and their contacts to demonstrate RDT sensitivity over time during early infection; index cases identified from routine campus-based testing. PCR+ve cases followed up (daily testing) for 14 days; contacts with all negative PCR results were followed up for 7 days.</p>	<p>Index test: Quidel SOFIA Ag using self-collected nasal swabs; laboratory-based direct testing the day after collection</p> <p>Reference standard: PCR (saliva and nasal swabs) and viral culture (PCR + nasal swabs)</p>	<p>‘Daily sensitivity’ of RDT or PCR in relation to time before or after first successful culture (from 2 days prior, to 13 days after)</p> <ul style="list-style-type: none"> • 2 days before viral culture positive (n = 10) <ul style="list-style-type: none"> ◦ 3, 30% RDT+; 8, 80% PCR+ve (direct saliva); 7, 70% PCR+ve (nasal) • 1 day before viral culture positive (n = 20) <ul style="list-style-type: none"> ◦ 8, 40% RDT+; 14, 70% PCR+ve (direct saliva); 14, 70% PCR+ve (nasal) • The day of first viral culture positive (n = 42) <ul style="list-style-type: none"> ◦ 38, 90.5% RDT+; 41, 97.6% PCR+ve (direct saliva); 42, 100% PCR+ve (nasal) • 1 day after viral culture positive (n = 43) <ul style="list-style-type: none"> ◦ 42, 97.7% RDT+; 43, 100% PCR+ve (direct saliva); 41, 95.3% PCR+ve (nasal)

Table 5. Studies evaluating repeated (serial) antigen testing (Continued)

Data reported for 43/51 PCR+ve; 8 without positive viral culture were excluded

- 2 days after viral culture positive (n = 43)
 - 40, 93.0% RDT+; 42, 97.7% PCR+ve (direct saliva); 43, 100% PCR+ve (nasal)
- 3 days after viral culture positive (n = 43)
 - 38, 88.4% RDT+; 41, 95.3% PCR+ve (direct saliva); 43, 100% PCR+ve (nasal)
- 4 days after viral culture positive (n = 43)
 - 27, 62.8% RDT+; 41, 95.3% PCR+ve (direct saliva); 43, 100% PCR+ve (nasal)
- 5 days after viral culture positive (n = 43)
 - 22, 51.2% RDT+; 35, 81.4% PCR+ve (direct saliva); 40, 93.0% PCR+ve (nasal)
- 6 days after viral culture positive (n = 43)
 - 19, 44.2% RDT+; 38, 88.4% PCR+ve (direct saliva); 38, 88.4% PCR+ve (nasal)
- 7 days after viral culture positive (n = 42)
 - 10, 23.8% RDT+; 29, 69.0% PCR+ve (direct saliva); 36, 85.7% PCR+ve (nasal)

Data used to model 'protocol sensitivities' of different testing strategies.* Probability of positive result before or during period when viral culture is positive was estimated as:

- daily testing: RDT 90.9% (20/22); direct saliva PCR 95.5% (21/22); nasal PCR 100% (22/22)
- every other day: RDT 84.1% (37/44); direct PCR 90.9% (40/44); nasal PCR 90.9% (40/44);
- every 3 days: RDT 80.3% (53/66); direct PCR 83.3% (55/56); nasal PCR 84.8% (56/66)

* 'protocol sensitivity' was reported as calculated using a value-of-information approach assuming seven different testing frequencies (from daily up to weekly sampling) (Smith 2021).

Winkel 2020

Players, staff and referees from 13 professional football clubs and the national teams in the Netherlands tested approximately weekly independent of presence of symptoms, 2 days prior to each match; results for symptomatic individuals were excluded

824 people provided 2425 samples; 52 positive on PCR (68 samples). 23/52 remained asymptomatic during testing period, 29/52 developed symptoms after 1st positive PCR test

Index: Abbott Panbio; NP swabs tested immediately by "trained personnel". Accuracy was calculated by either excluding results with weak test bands or by counting them as +ve or -ve to determine best and worst case scenarios.

Reference: single PCR (one of 3 assays used), genetic targets not reported; paired throat/ NP swabs used (104, 4% PCR swabs obtained on subsequent day)

Sensitivity and specificity calculated on a per-sample basis; samples reported during earlier phase of infection likely to be on par with per-patient results. Counting inconclusive results as RDT positive:

Sensitivity

- Pre-symptomatic (those with PCR+ve result prior to later onset of symptoms):
 - Se 91.7% (95% CI 61.5% to 99.8%) (11/12)
- Early infection (includes first PCR+ve result in asymptomatic plus any additional positives within 7 days of first positive PCR, regardless of symptoms):
 - Se 90.6% (95% CI 75.0% to 98.0%) (29/32)
- Late infection (≥ 7 days pso as long as symptoms had subsided or ≥ 7 days after 1st positive PCR):
 - Se 33.3% (95% CI 14.6% to 57.0%) (7/21)
- Persistent shedding (positive PCR > 4 weeks after the 1st positive PCR result):
 - Se 0.0% (95% CI 0.0% to 70.8%) (0/3)

Specificity: 99.5% (95% CI 99.2% to 99.8%) (2327/2338)

Table 5. Studies evaluating repeated (serial) antigen testing (Continued)

CI: confidence interval; **Ct:** cycle threshold; **N/A:** not applicable; **NHS:** National Health Service (UK); **NP:** nasopharyngeal; **PCR:** polymerase chain reaction; **PHE:** Public Health England; **pso:** post-symptom onset; **RDT:** rapid diagnostic test; **PCR:** reverse transcription polymerase chain reaction; **Se:** sensitivity; **Sp:** specificity

WHAT'S NEW

Date	Event	Description
21 July 2022	New citation required and conclusions have changed	New evidence incorporated; evidence for testing in asymptomatic cohorts has increased.
21 July 2022	New search has been performed	Updated with evidence published between September 2020 and March 2021.

HISTORY

Review first published: Issue 8, 2020

Date	Event	Description
10 January 2022	New search has been performed	Review updated with search until 18 March 2021.
15 April 2021	Amended	Clarification in Appendices that isothermal amplification is not a RT-PCR test.
24 March 2021	Amended	Correction of typo in abstract
24 March 2021	Amended	Amendment to PLS title
9 March 2021	New citation required and conclusions have changed	This review has been updated and the conclusions have changed
30 September 2020	New search has been performed	We have updated our review and now include 64 study reports in 78 study cohorts, evaluating 16 antigen and 5 molecular assays

CONTRIBUTIONS OF AUTHORS

JDi was the contact person with the editorial base.

JDi co-ordinated contributions from the co-authors and wrote the final draft of the review.

JDi, PS, SvW, MT screened papers against eligibility criteria.

RS conducted the literature searches.

JDi, PS, SvW, NN, CD, JDo, JB, MT appraised the quality of papers.

JDi, PS, SvW, NN, CD, JDo, JB, MT extracted data for the review and sought additional information about papers.

JDi, PS entered data into [Review Manager 2020](#).

JDi, SB, JJD, YT, CD analysed and interpreted data.

JDi, JJD, YT, CD, STP, RS, ML, MM, LH, AVB, DE, SD, JC, JV worked on the methods sections and commented on the draft review.

JDi, CD, YT responded to the comments of the referees.

JDi is the guarantor of the update.

DECLARATIONS OF INTEREST

Jonathan J Deeks: JD has published or been quoted in opinion pieces in scientific publications, and in the mainstream and social media related to diagnostic testing. JD was the statistician on the Birmingham evaluation of the Innova test which is mentioned in the discussion of the paper. There was no funding for this evaluation of the Innova test. JD is a member of the Royal Statistical Society (RSS) COVID-19 taskforce steering group, and co-chair of the RSS Diagnostic Test Advisory Group. He is a consultant adviser to the World Health Organization (WHO) Essential Diagnostic List. JD receives payment from the BMJ as their Chief Statistical advisor.

Jacqueline Dinnes: none known

Yemisi Takwoingi: none known

Clare Davenport: none known

Mariska MG Leeflang: none known

René Spijker: none known

Lotty Hooft: none known

Ann Van den Bruel: none known

Devy Emperador: is employed by FIND with funding from DFID and KFW. 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.

Sabine Dittrich: is employed by FIND with funding from DFID and Australian Aid. 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.

Sian Taylor-Phillips: none known

Sarah Berhane: none known

Jane Cunningham: none known

SOURCES OF SUPPORT

Internal sources

- Liverpool School of Tropical Medicine, UK
- University of Birmingham, UK

External sources

- Foreign, Commonwealth, and Development Office (FCDO), UK

Project number: 300342-104

- National Institute for Health Research (NIHR), UK
- NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, UK

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

As the evidence base evolves over the course of the pandemic, we have made some adjustments to our original approach with the following changes between earlier versions of the review and this second update:

- Clarification regarding inclusion criteria: restricted to studies evaluating commercially produced rapid antigen tests; a separate review update covering rapid molecular tests is planned

Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection (Review)

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- Search sources included in the protocol and the previous versions of this review, the Cochrane COVID-19 Study Register and the CDC Database of COVID-19 Research Articles, were not included in this version as the single source from the University of Bern living search database proved more efficient to process as it did not involve manual effort to deduplicate.
- We planned to check the following websites for eligible index tests, however these did not prove to be very accessible or easy to use and, after initial review, were not further considered:
 - National Institute for Health Research (NIHR) Innovation Observatory (www.io.nihr.ac.uk/)
 - www.rapidmicrobiology.com/test-method/testing-for-the-wuhan-coronavirus-a-k-a-covid-19-sars-cov-2-and-2019-ncov
 - Meta-evidence (meta-evidence.co.uk/the-role-of-evidence-synthesis-in-covid19/)
- Electronic sources searched for previous review updates were dropped, including:
 - Cochrane COVID-19 Study Register; not searched since 28 March 2020 because of lack of coverage of preprint literature
 - the 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); the Norwegian Institute of Public Health 'NIPH systematic and living map on COVID-19 evidence' (www.norgesk.no/forskningskart/NIPH_diagnosisMap.html); not searched since 15 Nov 2020 because of the move to a review-specific classifier approach and availability of more directly relevant sources of eligible primary studies as documented in [Searching other resources](#).
- We intended for two authors to independently perform data extraction, however one review author extracted study characteristics, and a second author checked them. Contingency table data were extracted independently by two review authors as planned.
- We planned to evaluate the effect of additional sources of heterogeneity, including reference standard. However, additional formal investigations using meta-regression were not possible because of lack of variability across the studies in these features.
- We planned to conduct a sensitivity analysis excluding studies that are solely published as preprints. We have inadequate study numbers to allow this at present but will reconsider for the next update.

INDEX TERMS

Medical Subject Headings (MeSH)

*COVID-19 [diagnosis]; COVID-19 Testing; Pandemics; Point-of-Care Systems; SARS-CoV-2; Sensitivity and Specificity

MeSH check words

Humans