Should rapid antigen tests be used as a screening tool for COVID-19?

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This rapid review summarizes the available evidence on the diagnostic accuracy of rapid antigen tests (RAgTs) for COVID-19. Conclusions may change as new evidence becomes available.

KEY FINDINGS

Based on moderate quality evidence, the use of rapid antigen tests as a screening tool for COVID-19 is limited by its low sensitivity. Because of its overall low sensitivity and the high uncertainty on its accuracy, we recommend limiting its use for diagnosis confirmation when RT-PCR is not available and for patients with high pre-test probability, such as suspected cases in hospitals. High quality validation studies are needed.

- Rapid antigen tests (RAgT) are point-of-care tests used to detect a viral infection. Due to its practicality, RAgTs are currently being explored as a screening and/or diagnostic tool for COVID-19.
- Nine studies evaluating 7 RAgT brands were found. 12 clinical validation studies are ongoing.
- RAg tests have high specificity of 99% (95% CI: 98 to 100) but a low sensitivity of 49% (95%CI: 28 to 70).
- Sensitivity estimates ranged from 0 to 94% in different studies and may have been affected by the study design, brand used, population being tested, reference standard or specimen used, and day of illness when the test was done.
- More studies are needed to clarify the role of RAgT before government agencies invest in these diagnostic tests.
- WHO currently does not recommend the use of RAgT in patient care but encourages more research on them. US-NIH allows its use but warns of possible false negatives.

BACKGROUND

Rapid antigen detection tests (RAgT) are point-of-care tests used to detect viral infections. Most RAgTs detect the presence of a virus through an immunochromatographic assay that gives out color upon detection of a target viral protein. Samples being analyzed are mostly from nasopharyngeal specimens. Due to their ease of use, limited technical and infrastructural requirements, and ability to render quick results, several RAgTs have been produced and are currently being explored as screening and/or diagnostic tests for COVID-19 (La Marca 2020).

The diagnostic accuracy of RAgTs for COVID-19 compared to more acceptable diagnostic tools such as RT-PCR needs to be determined before deciding if it can be integrated in the existing algorithm of care or public health policy for COVID-19. This systematic review aims to synthesize available evidence on the diagnostic accuracy of RAgT for COVID-19.

Objectives

To determine the diagnostic accuracy of rapid antigen tests compared to RT-PCR in screening for COVID-19

Secondary objectives

To explore diagnostic accuracy of rapid antigen tests stratified according to:

a. test brand/manufacturer
b. presence of symptoms
c. duration of symptoms
d. type of specimen used

METHODS

Criteria for considering studies for this review

Types of studies

We included published and preprint studies that reported the diagnostic performance data of any RAgT for SARS-CoV-2 and used RT-PCR as the reference standard. These involved diagnostic cross-sectional, cohort, or case-control study designs. Other study types were included if they provided data that allowed computation of diagnostic accuracy measures.

Participants

We included studies that recruited participants of any age, COVID-19 status, symptom severity, risk of exposure, and setting. Studies that used stored laboratory specimens from patients were also included.

Index tests

We included novel, RAgTs detecting recombinant SARS-CoV-2 antigens that were listed in the FIND SARS-CoV-2 Diagnostic Pipeline (https://www.finddx.org/covid-19/pipeline/) or have obtained regulatory approval from the Philippine Food and Drug Administration (FDA) (https://www.fda.gov.ph/covid-19-fda-updates/). As of August 17, 2020, there are already 8 RagT brands that are approved by the Philippine FDA. Studies that used RAgTs that are not yet commercially available were excluded.

Target conditions

Studies must have identified any of the following as target conditions: mild to moderate COVID-19, COVID-19 pneumonia, suspected or confirmed current SARS-CoV-2 infection, past SARS-CoV-2 infection, or asymptomatic SARS-CoV-2 infection.

Reference standard

Real Time – Polymerase Chain Reaction (RT-PCR) was considered as the reference standard regardless of whether it was used alone or in combination with imaging (e.g., chest CT), clinical evaluation, or current WHO case definitions for COVID-19. No restrictions were applied in terms of specimen used, brand/manufacturer, or diagnostic threshold (cycle threshold or Ct value).

Search methods for identification of studies

Electronic searches

We conducted a literature search for studies published in 2019 to 2020 on MEDLINE using subject headings combined with text words related to COVID-19 or SARS-CoV-2 and rapid antigen tests/testing, with no language limits or method filters. To identify preprint studies, we searched the COVID-19 Living Evidence Database using "antigen" as the search term (https://zika.ispm.unibe.ch/assets/data/pub/search_beta/). This database is updated daily and includes preprints from medRxiv and bioRxiv as well as published articles from EMBASE and Pubmed. The Cochrane COVID-19 Study Register (covid-19.cochrane.org/) was also searched using "antigen" as a search term. The final search date was done on 15 August 2020.

Table 1 details the full search strategy for MEDLINE.

Searching other resources

To supplement the yield from the initial search, available data on RAgT from FIND SARS-CoV-2 Diagnostic pipeline (https://www.finddx.org/covid-19/dx-data/) was accessed. This repository was last updated on 30 July 2020. References of all included studies were also reviewed for possible inclusion. Reported sensitivity and specificity estimates from the package inserts of RagTs approved by the Philippine FDA were also retrieved but were not included in the main analysis. Relevant clinical trials were searched on clinicaltrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP).

Data collection and analysis

Selection of studies

Two researchers independently screened study titles and abstracts. Disagreements were resolved by consensus or by consulting a third review author.

Data extraction and management

Two researchers independently performed data extraction for all included studies. Data on study information (country, test setting, date, funding source), population (number, symptom severity, onset of symptoms), reference standard (RT-PCR brand, specimen used, diagnostic threshold set), index test (name of antigen test, manufacturer, test use case, specimen used, method of interpretation, target antigen), and diagnostic performance data (true and false positives, true and false negatives, sensitivity, specificity, etc.) were collected. Authors were contacted by email to clarity details or to obtain missing information.

Assessment of methodological quality

Two review authors independently assessed risk of bias of the included studies and applicability concerns using the QUADAS-2 tool (Whiting 2011). Disagreements were resolved by discussion until a consensus rating was obtained.

Statistical analysis and data synthesis

Data from each study were extracted to produce 2x2 contingency tables:

		RT-PCR	
		Positive	Negative
Rapid Antigen Test	Positive	**True Positive (TP)**	**False Positive (FP)**
	Negative	**False Negative (FN)**	**True Negative (TN)**

We determined the sensitivity and specificity together with confidence intervals for each of the tests and presented them in paired forest plots and summary tables. Dumbbell plots were also created to visualize the change in disease probability after a positive or negative RagT result. Overall pooled sensitivity and specificity estimates were derived using a bivariate mixed-effects binary regression model (Dwamena 2007). All statistical analyses were performed using Stata 15.0. (TX, USA: StataCorp LLC, 2019). Data were organized using Review Manager (RevMan) 5.4 (Cochrane Collaboration, 2020).

Investigations of heterogeneity

Heterogeneity was determined by visual inspection of the forest plots. Because of anticipated heterogeneity across studies, we derived pooled sensitivity and specificity estimates by stratifying studies according test brand, type of specimen used, and participant characteristics. A univariate

random-effects model was used due to the limited number of studies (< 4) available per brand (Takwoingi 2015).

Sensitivity analyses

Sensitivity analysis was performed by removing studies with low methodologic quality and assessing their impact on overall diagnostic accuracy estimates.

Results

Results of the search

Included Studies

Figure 1 shows a flow diagram summarizing the results of the literature search, number of excluded and included studies, and reasons for exclusion. **Table 2** summarizes the main characteristics of all included studies.

Overall, 408 records (322 unique) were identified from primary databases and additional sources. Nine studies met the inclusion criteria. Among the included studies, 3 were preprints (Diao 2020; Herrera 2020; Weitzel 2020). One published study was excluded as it did not perform confirmatory RT-PCR to 39/774 patients who tested positive on RAgT (Blairon 2020).

Seven different RAgT brands were evaluated across all 9 studies. One study performed a head-to-head comparison of 4 RAgT brands (Weitzel 2020). There were 3 studies from Europe (Lambert-Niclot 2020; Mertens 2020; Scohy 2020), 2 from Chile (Porte 2020; Weitzel 2020), 2 from China and Hong Kong (Diao 2020; Mak 2020), 1 from Japan (Nagura-Ikeda 2020), and 1 from USA (Herrera 2020). Of the 7 RAgTs investigated, 2 produce results that are automatically read by a fluorescence immunoassay analyser (Sofia 2 SARS Antigen FIA, Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit) while the rest relied on visual interpretation by a reader.

A total of 2,763 patients (median n = 133; range: 19 –1172) were included across 9 studies. Seven studies involved symptomatic or suspected COVID-19 patients, while 3 studies included both symptomatic and asymptomatic patients (Nagura-Ikeda 2020; Porte 2020; Scohy 2020). In the studies that had available information regarding participants, majority of the viral antigen testing was done within the first week of symptom onset. Healthcare workers were included in two studies (Herrera 2020; Mertens 2020). Two studies used only SARS-CoV-2-positive samples and sensitivity estimates (Mak 2020; Nagura-Ikeda 2020). All studies used RT-PCR testing as the reference standard with 5/9 using nasopharyngeal swab specimens. Two studies (Porte 2020; Nagura-Ikeda 2020) segregated data on diagnostic accuracy according to timing of testing in relation to symptom onset.

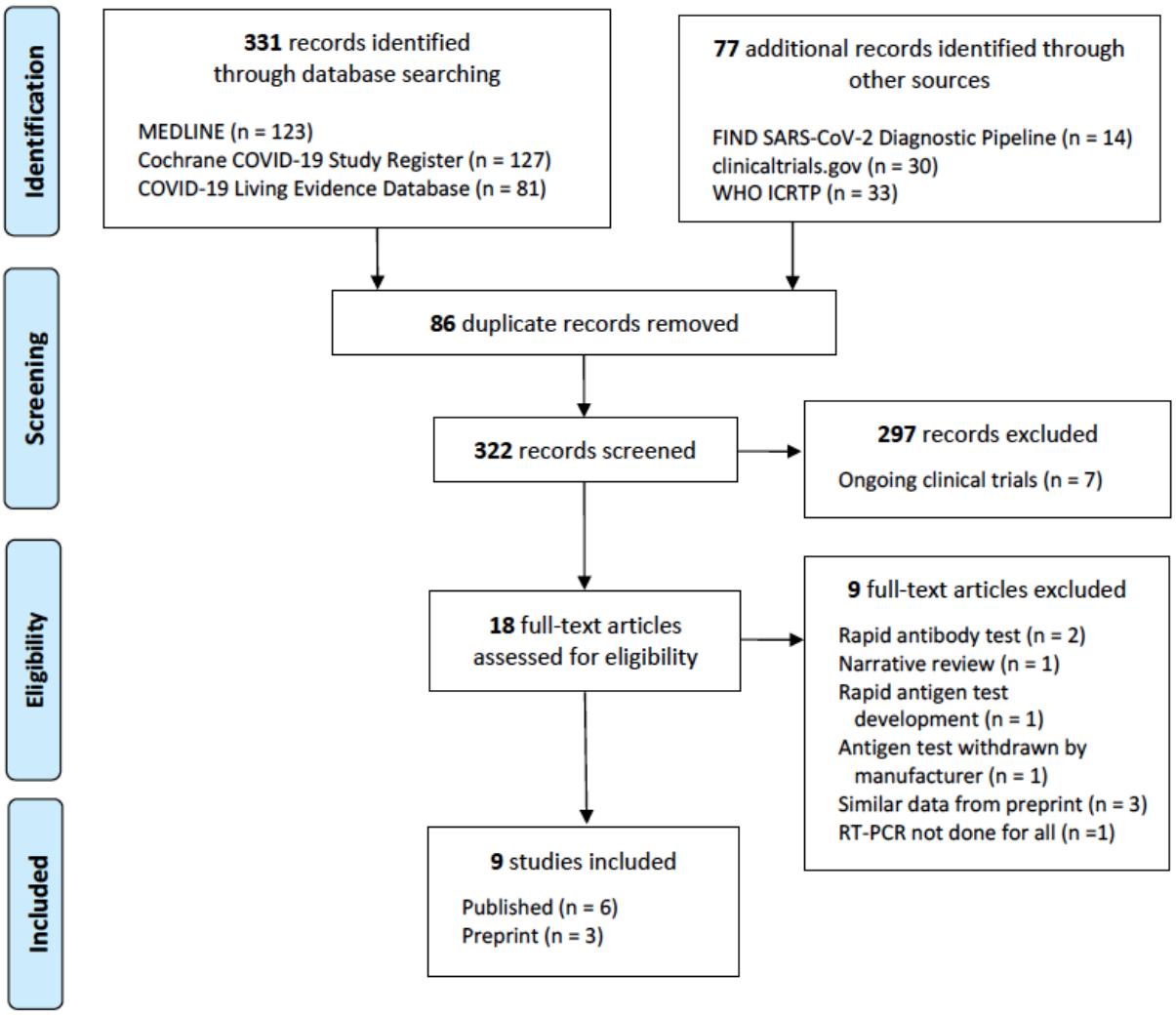

Figure 1. Study flow diagram.

Methodological quality of included studies

Figures 2 and 3 summarize the results of the quality assessment using QUADAS-2. Overall methodological quality of included studies is rated moderate. Quality was rated as high in 1 study (Diao 2020), moderate in 4 studies (Herrera 2020; Lambert-Niclot; Porte 2020; Weitzel 2020), low-to-moderate in 2 studies (Mertens 2020; Scohy 2020), and low in 2 studies (Mak 2020; Nagura-Ikeda 2020).

For the participant selection domain, an unclear risk of bias was seen in 5/9 (56%) studies as a result of using convenience sampling for selecting specimens for testing (Porte 2020; Weitzel 2020) or insufficient reporting of characteristics of included participants/samples or sampling methods (Herrera 2020; Lambert-Niclot 2020; Mak 2020). These may have led to an over- or underrepresentation of patients with particular characteristics (e.g., individuals with symptoms or comorbidities, patients on the late phase of infection). Since we considered RAgTs to be used for point-of-care testing, applicability concerns were rated as unclear in 2 studies that used data stored in sample banks (Lambert-Niclot 2020; Mak 2020).

For the index test domain, 2/10 studies (Mak 2020; Nagura-Ikeda 2020) were concluded to have high risk of bias since they applied RAgTs that depend on subjective interpretation of visual readouts among samples that were all known to be positive for SARS-CoV-2 on RT-PCR. Three studies (Lambert-Niclot 2020; Mertens 2020; Scohy 2020) that used an RAgT with visual readout (COVID-19 Ag Respi-Strip) were rated as having unclear risk of bias as they did not specify if RAgT results were interpreted without knowledge of RT-PCR results. Two studies (Weitzel 2020; Mak 2020) used modified processing methods for RAgT specimens by not using the manufacturer-recommended test solutions, which raises concern regarding the index tests' applicability in other settings. All included studies posed low risk for bias related to the reference standard domain.

Risk of bias related to flow and timing was judged as low in only 3/9 studies (Diao 2020; Lambert-Niclot 2020; Porte 2020). Studies that involved a gap of at least 24 hrs or did not specify the duration of time interval between RT-PCR and RAgT testing were rated as having an unclear risk of bias (Mak 2020; Mertens 2020; Scohy 2020; Weitzel 2020), owing to the possible effect of time delay on the integrity of the specimens or on the accuracy of interpretation of results. In one study, saliva specimens for RAgT were collected from patients after an average of 3 days after receiving their first positive RT-qPCR result (Nagura-Ikeda 2020). This introduced a high risk of bias since viral load is known to change rapidly over the course of days.

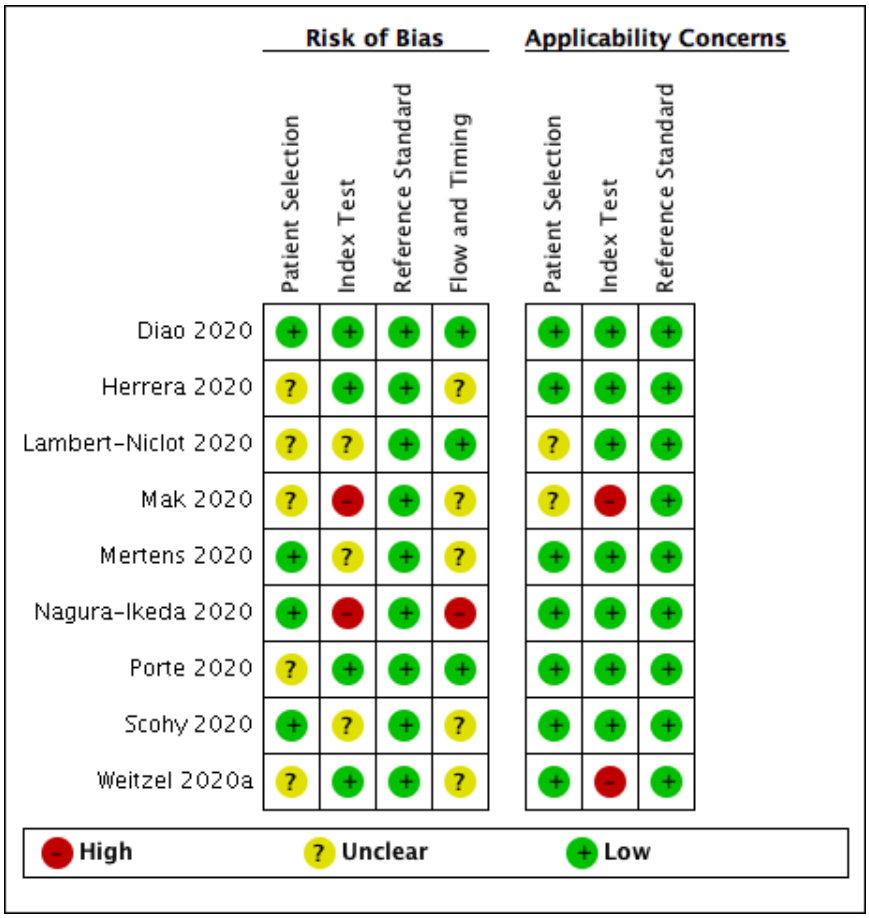

Figure 2. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study

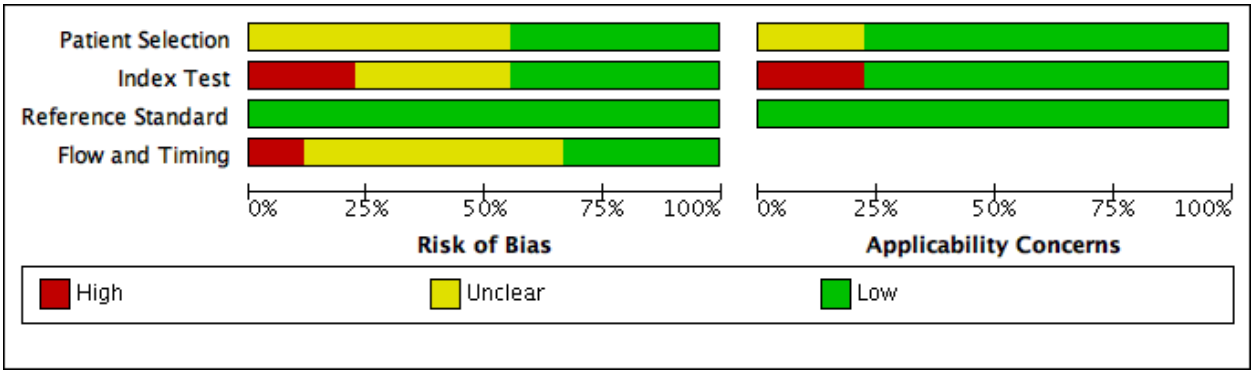

Figure 3. Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies

Diagnostic Accuracy Findings

Overall, the pooled sensitivity of RAgTs is 49% (95%CI: 28, 70) (**Figure 4**). The sensitivity of the RAgTs varied widely across different test brands and study populations, ranging from 0 to 94%. In contrast, the specificity of RAgTs remained consistently very high in all studies, with a pooled specificity of 99% (95% CI: 98, 100). The sensitivity, specificity, predictive values, and likelihood ratios for each study and test are summarized in **Table 2**.

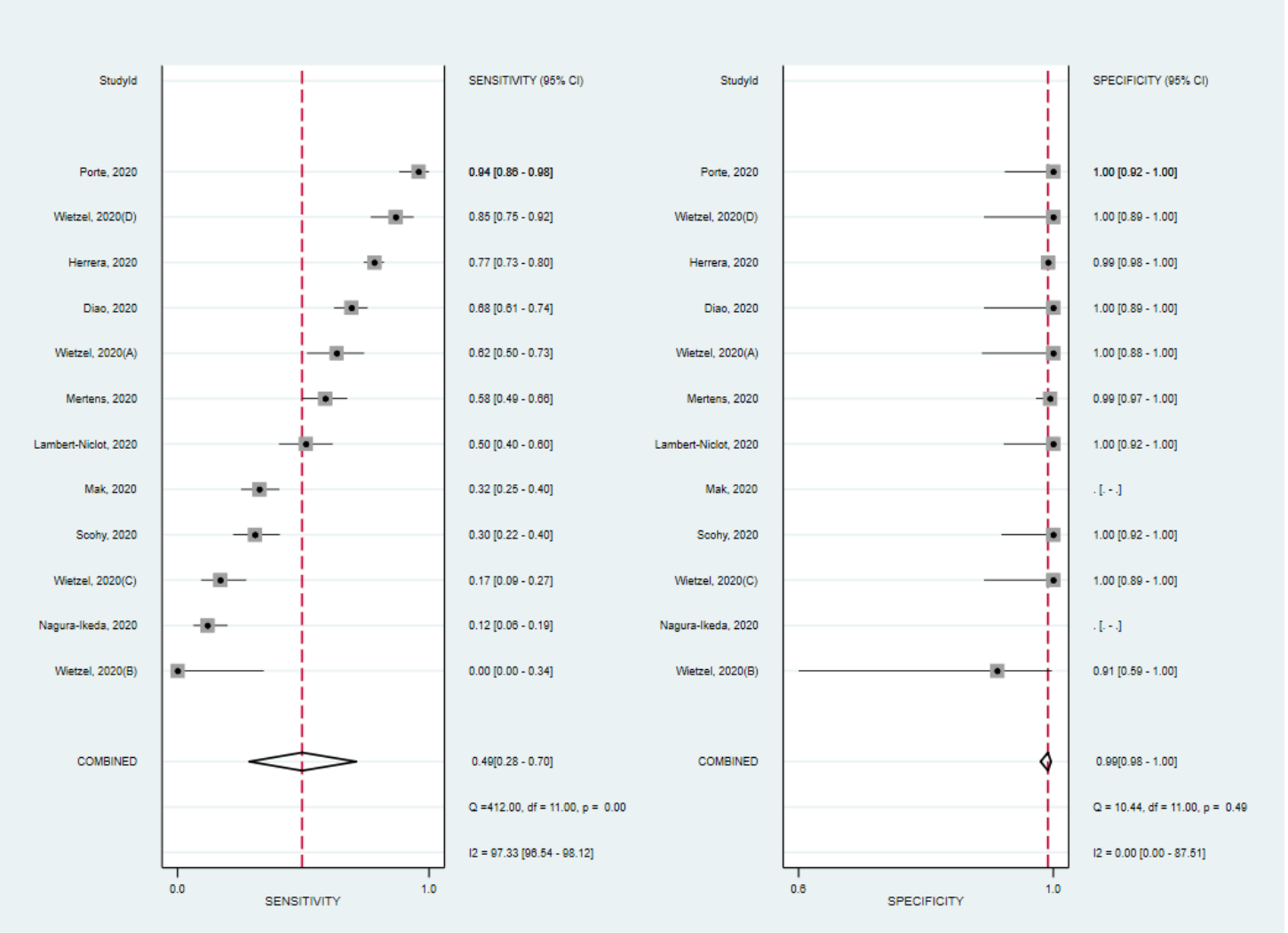

Figure 4. Paired forest plots showing individual and pooled sensitivity and specificity estimates of rapid antigen tests for SARS-CoV-2. Diagnostic accuracy data were obtained for 7 rapid antigen test brands, with 1 study (Weitzel 2020) evaluating four different brands.

Subgroup analysis

Substantial heterogeneity for sensitivity estimates was observed upon visual inspection of forest plots. Thus, we explored factors affecting the sensitivity of RAgTs. Results of these investigations for heterogeneity are summarized in **Table 3**.

a. Effect of test brand

Sensitivity estimates were different across test brands and within studies evaluating the same brand (**Figure 5**). Based on 3 studies (n = 614) with moderate to high methodological quality, the Bioeasy 2019-nCov Ag Fluorescence Rapid Test Kit showed the highest pooled sensitivity (Sn = 82.3; 95% CI: 66, 98.5), followed by the Sofia 2 SARS Antigen FIA (Sn= 76.7; 95% CI: 72.6, 80.3) in one study involving 1,172 patients. The sensitivity of the remaining 5 RAgTs were all below 50%.

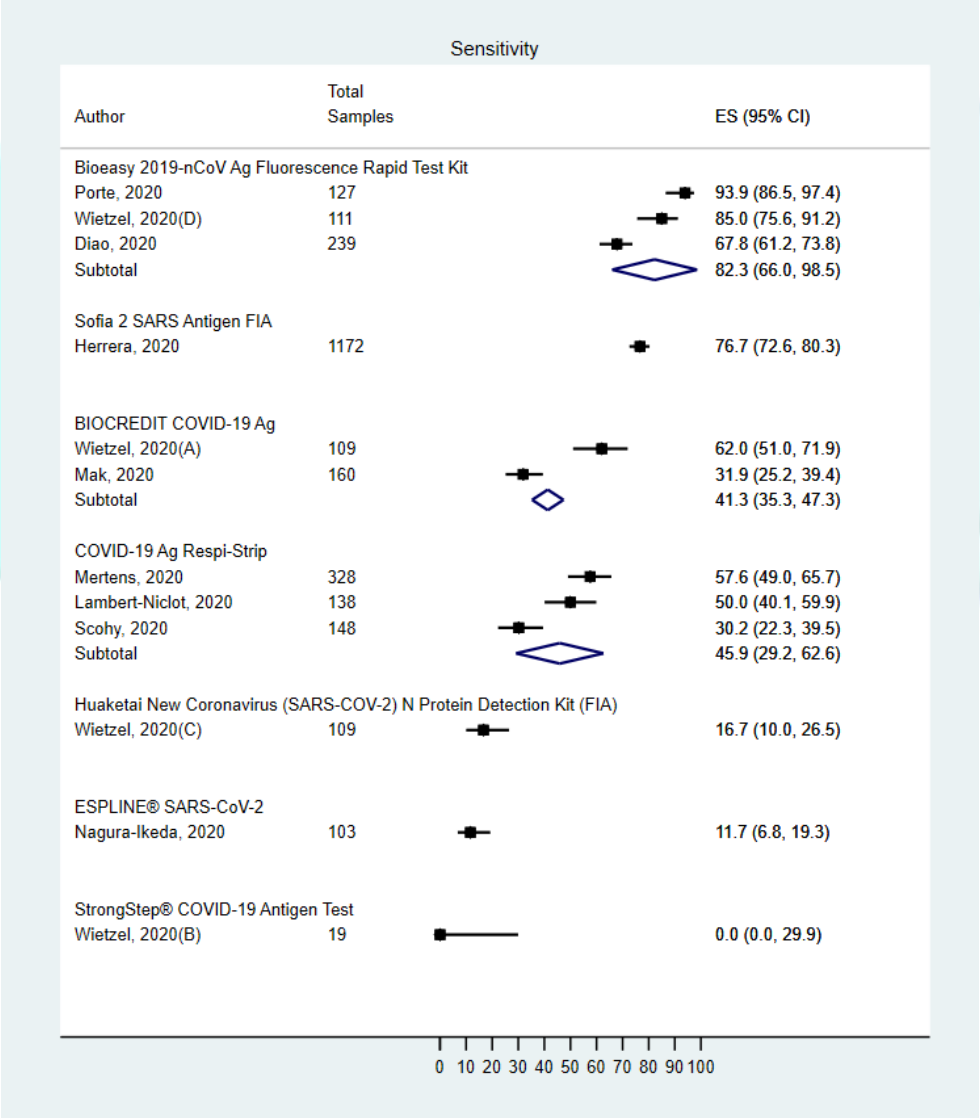

Figure 5. Sensitivity of rapid antigen tests according to brand.

b. Effect of symptom presence

The pooled sensitivity of RAgTs was higher among symptomatic patients (n = 2,388) reported in 7 studies (Sn = 50.3; 95%CI 20, 80.7) compared to asymptomatic patients (n = 60) in 2 studies (Sn = 18.6; 95%CI 4.7, 32.5) (**Figure 6**).

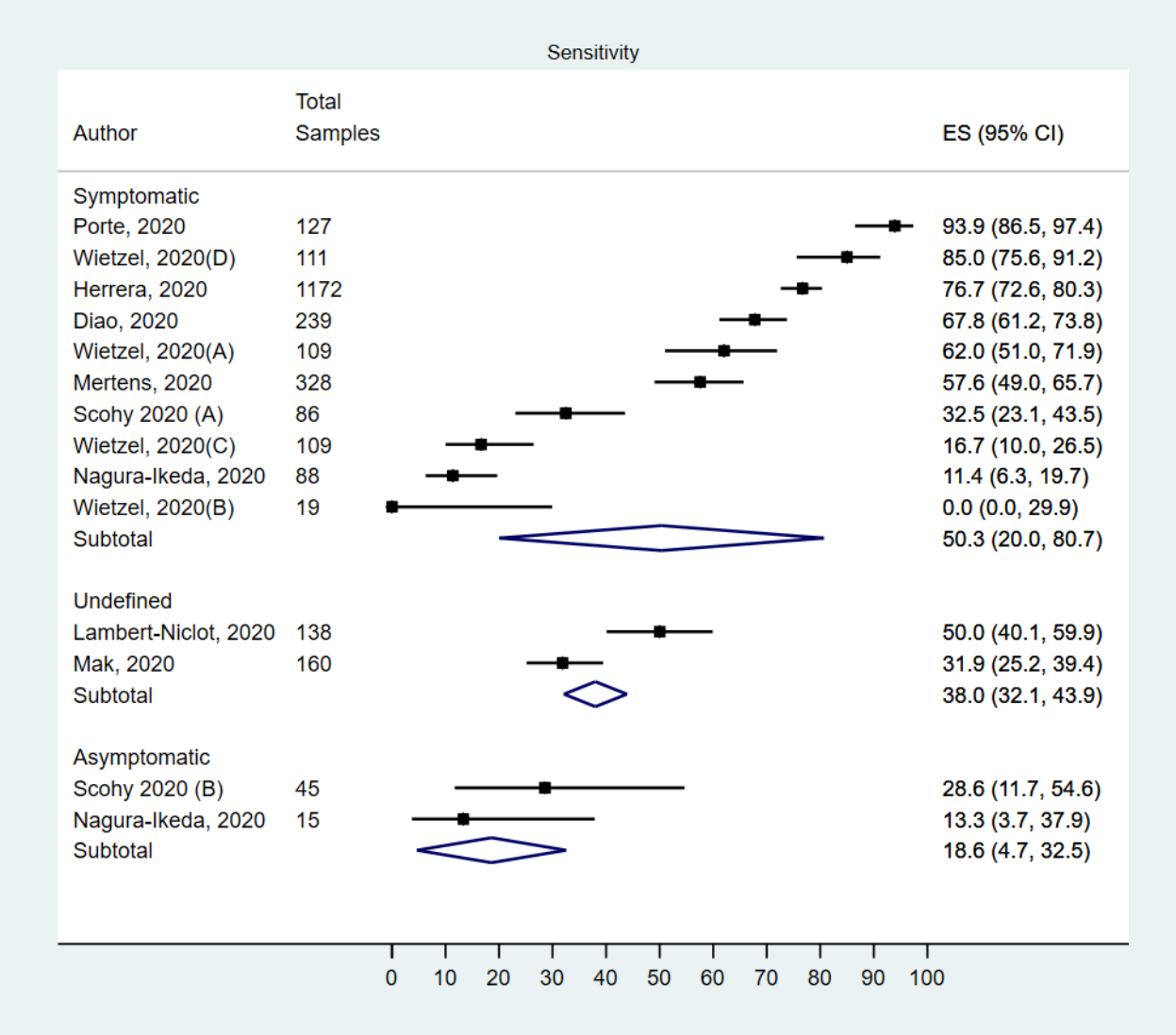

Figure 6. Sensitivity of rapid antigen tests in symptomatic versus asymptomatic patients with COVID-19.

c. Effect of time of testing in relation to onset of symptoms

RAgTs exhibited a higher pooled sensitivity of 43.1% (95%CI: 6.3, 79.8) for patients tested in the early phase of the disease (0-7 days; n = 675) as compared to those who were tested late (8-14 days; n = 35) with a pooled sensitivity of 12.7% (95%CI: 3.2, 22.3) (**Figure 7**). However, the total sample sizes for asymptomatic patients and patients in the late phase of infection were too small

to make definitive conclusions. The studies that tested asymptomatic patients were also different in terms of specimen used (saliva vs nasopharyngeal swab).

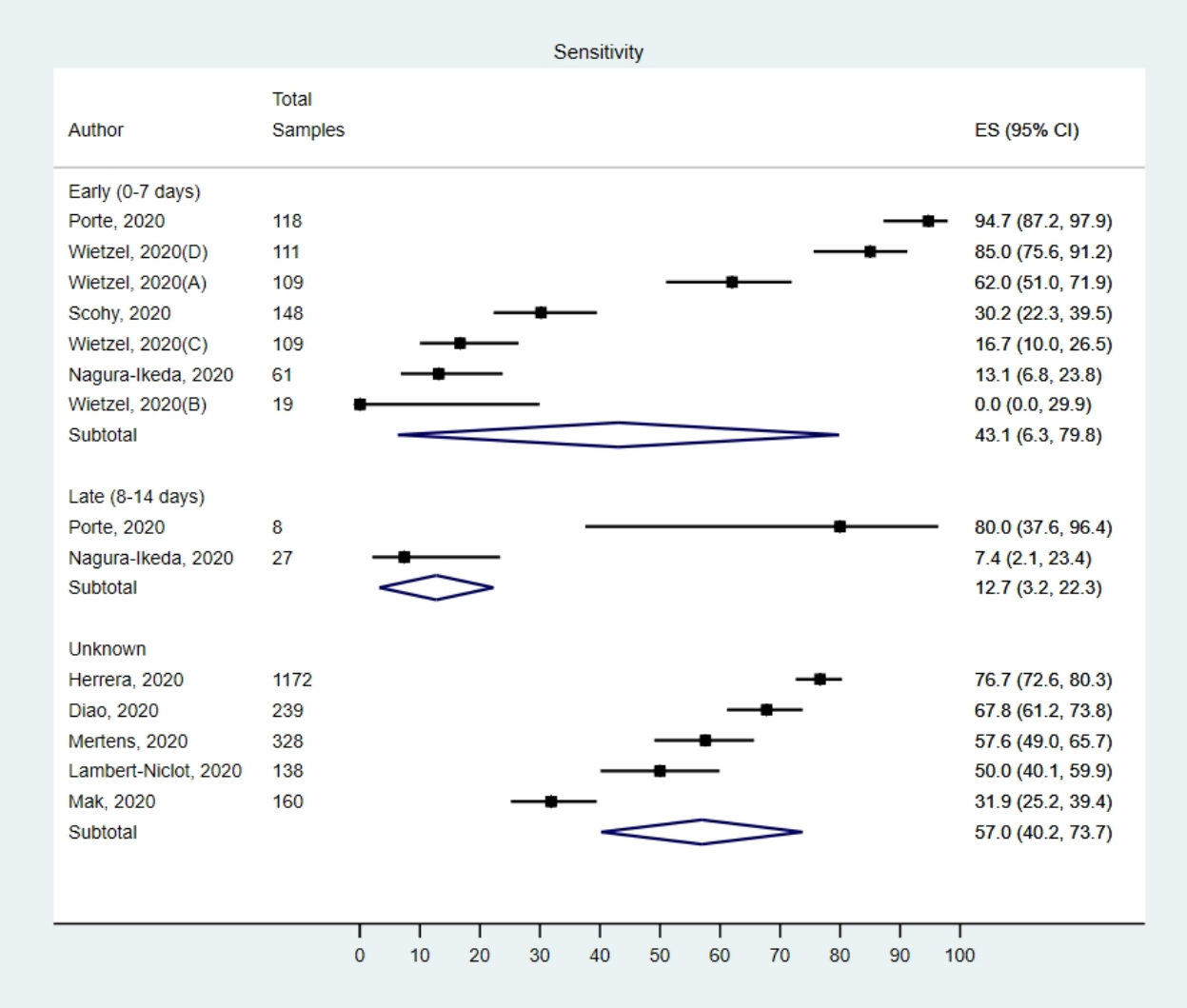

Figure 7. Sensitivity of rapid antigen tests by phase of the disease.

d. Effect of type of specimen used

RAgTs that used nasopharyngeal swab specimens alone had the highest pooled sensitivity of 56.7% (95%CI 40.8, 72.7) in five studies (n = 2,025) followed by combined nasopharyngeal and oropharyngeal swab (Sn = 50.5%; 95% CI 6.9, 94.7) in 3 studies (n = 510) (**Figure 8**). On the other hand, RAgTs using sputum as a specimen had a lowest pooled sensitivity of 11% (95%CI 4, 24).

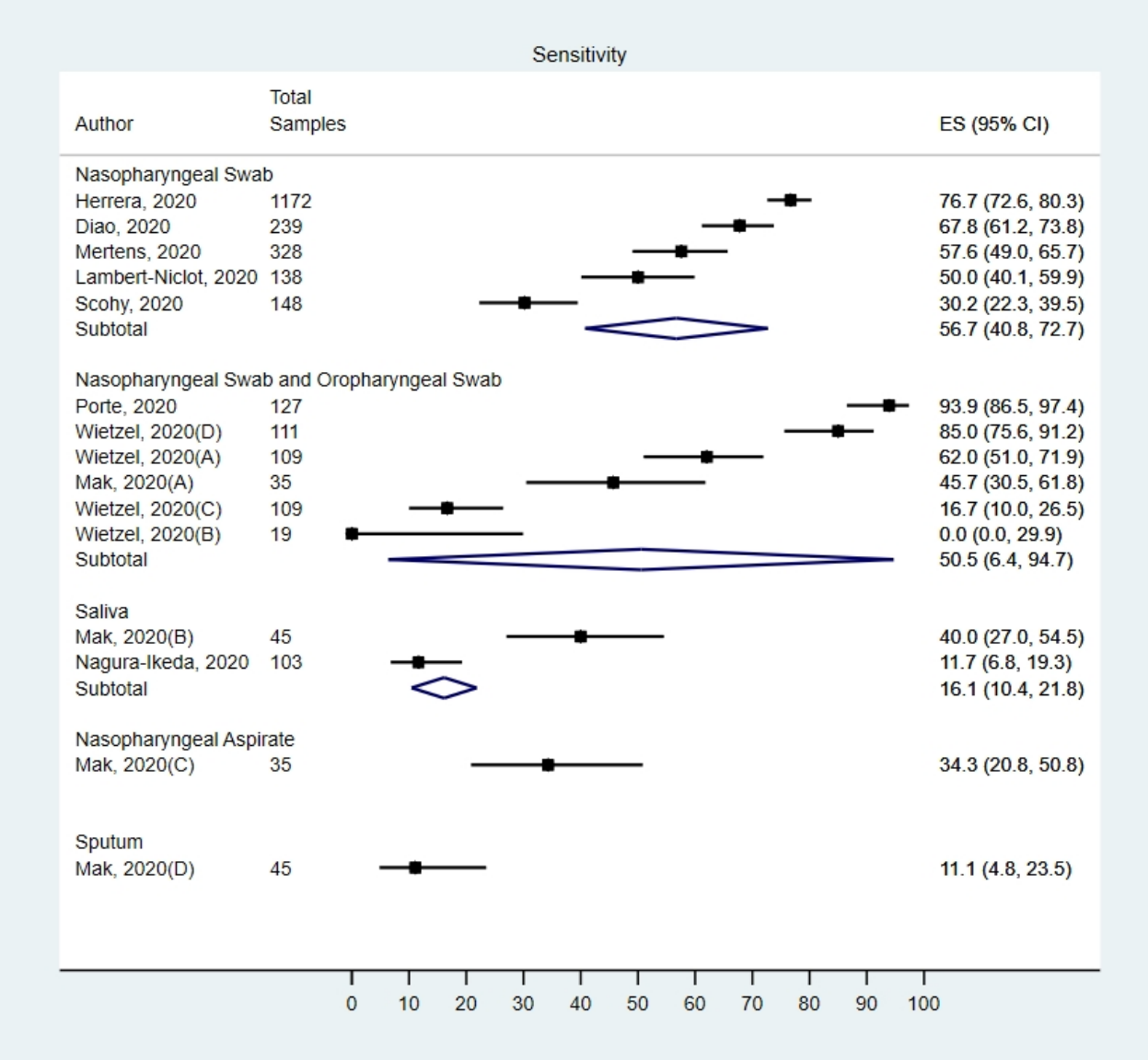

Figure 8. Sensitivity of rapid antigen tests by type of specimen used.

e. Other factors

Changing the diagnostic threshold value for RT-PCR (cycle threshold [Ct]) also affected the resulting sensitivity of the RAgTs. One study reported that changing the Ct value from ≤ 40 to ≤ 30 resulted in an increase of sensitivity from 68% (95% CI: 61, 74) to 98% (95% CI: 90, 100), demonstrating the impact of testing samples with higher viral loads.

Sensitivity analysis

Upon removal of 4 studies rated with low methodologic quality, the overall sensitivity estimate (49%) increased slightly to 57% (95%CI: 23, 93) but still remained low.

Ongoing Studies

There are at least 12 ongoing clinical validation studies on RAgTs in the trial registries and FIND (**Table 4**). Seven clinical trials (1 recruiting, 6 planned) were found: 2 from France (TRODVID19, NCT04337996; ERap-COV, NCT04405492-E), 1 each from Germany (DRKS00021220), UK (SOCRATES, NCT04403906), USA (NCT04348864), Japan (UMIN000040386), and India (CTRI/2020/07/026369). All 7 trials aim to include symptomatic adults with suspected or confirmed COVID-19 and evaluate the diagnostic accuracy of a rapid antigen test using RT-PCR as reference standard. Ease of use for self-testing, cost, and efficiency were also included as secondary outcomes. The average number of participants for these trials is 300 (range: 100 - 2,000). As of this writing, FIND is validating 5 RAGT brands, namely (1) COVID-19 Ag Respi-Strip, (2) BIOCREDIT COVID-19 Ag, (3) STANDARD F COVID-19 Ag FIA, (4) STANDARD Q COVID-19 Ag Test, and (5) Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit (FIND, 2020)

Discussion

Summary of main results

The sensitivity of RAgTs greatly varies, ranging from 0 to 94%. The pooled sensitivity of 49% implies that RAgTs have a high false negative rate. On the other hand, the specificity of RAgTs remained consistently very high at 99% across all studies. Caution should be taken when interpreting our findings especially for pooled estimates for sensitivity as there was substantial heterogeneity seen across studies.

We observed that the sensitivity of RAgT is highly brand-dependent, which may be due to differences in mode of interpretation of test results or the reagents used. In particular, RagTs that made use of automated readers for determining a positive or negative result, such as the Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit and Sofia 2 SARS Antigen FIA, appeared to have higher sensitivity compared to those which depended on visual readouts.

Sensitivity estimates were higher among symptomatic compared to asymptomatic participants. However, the impact of applying RAgT for asymptomatic patients still warrants further investigation as the number of asymptomatic patients involved in this review was too small to allow definitive conclusions to be made.

Testing patients early in the disease process also appeared to increase the sensitivity of RAgTs. This finding appears to be reflective of the effect of viral load on the accuracy of antigen tests. Previous investigations related to the temporal profile of SARS-CoV-2 viral loads shows that it peaks at the onset of symptoms and gradually decreases thereafter (He 2020; To 2020; Zou 2020).

RAgT using nasopharyngeal swab specimens had the highest sensitivity but did not appear to differ significantly from those that make use of combined nasopharyngeal and oropharyngeal swab specimens. This finding is consistent with a previous study on respiratory viral infections showing that combined nasopharyngeal and oropharyngeal swab specimens showed little added benefit compared to nasopharyngeal swab alone (Dawood 2015). Another study also showed the advantage of nasopharyngeal over oropharyngeal swab specimens in terms of sensitivity in detecting COVID-19 (Wang 2020).

Strengths and weaknesses of the review

Since most studies only focused on evaluating the diagnostic accuracy of a single brand, the effect of confounding factors should always be considered when attempting to compare accuracy of different test brands. Ideally, a bivariate model should have been used in pooling diagnostic test accuracy. However, a univariate model was used due to limited studies found. This, together with the significant heterogeneity observed across studies, may have result in imprecision with our reported overall pooled estimates. While we identified possible sources of heterogeneity affecting the sensitivity of RAgTs, the analyses we performed are only preliminary and must be verified by future studies.

Applicability of findings to the review question

To demonstrate the clinical utility of rapid antigen tests, we computed for the post-test probabilities associated with each test brand under three possible scenarios: (a) asymptomatic patients, (b) symptomatic patients in a community setting, and (c) symptomatic patients in a hospital setting. In all scenarios, the pooled sensitivity of 49% was used.

a. **Asymptomatic patients:** Assuming a 1% pre-test probability for asymptomatic COVID-19 patients, the post-test probability of an asymptomatic patient who tests positive on RAgT will increase to 34%, but will not change in case of a negative RAgT result (**Figure 8)**.

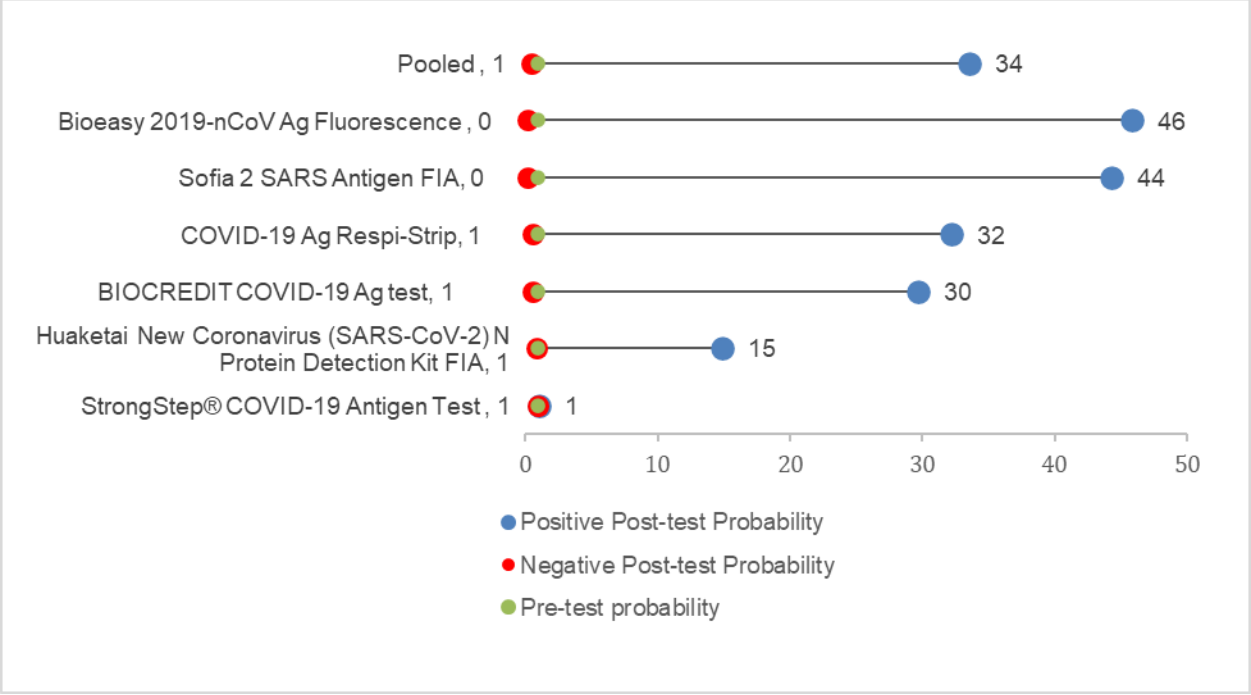

Figure 8. Dumbbell plot showing the post-test probabilities for asymptomatic patients. Pretest probability was assumed to be 1%.

b. **Symptomatic patients, community setting:** Assuming a 10% pre-test probability for symptomatic COVID-19 patients and a pooled sensitivity of 49%, a symptomatic patient will have a positive post-test probability of 85% and negative posttest probability of 5%

(**Figure 9)**.

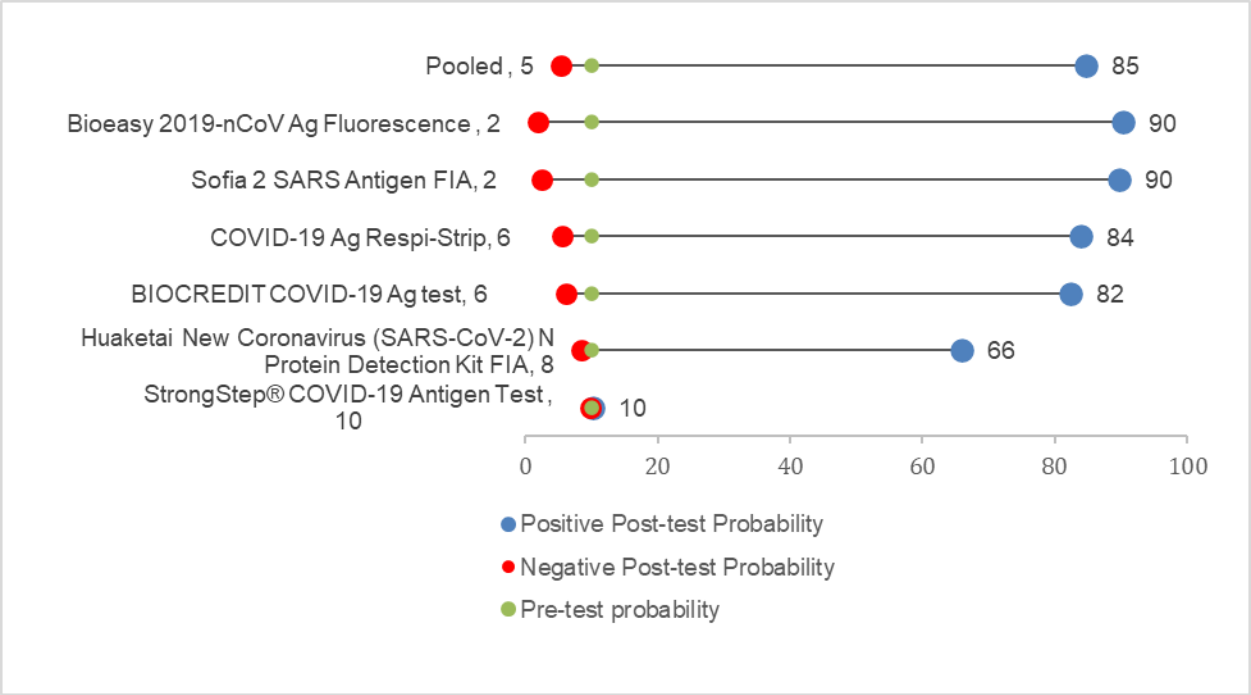

Figure 9. Dumbbell plot showing the post-test probabilities among symptomatic patients in the community. Pretest probability was assumed to be 10%.

c. **Symptomatic patients, hospital setting:** Assuming a 40% pre-test probability for symptomatic COVID-19 patients presenting in hospitals, a symptomatic patient will have a positive post-test probability of 97% and a negative posttest probability of 25%. (**Figure 10**).

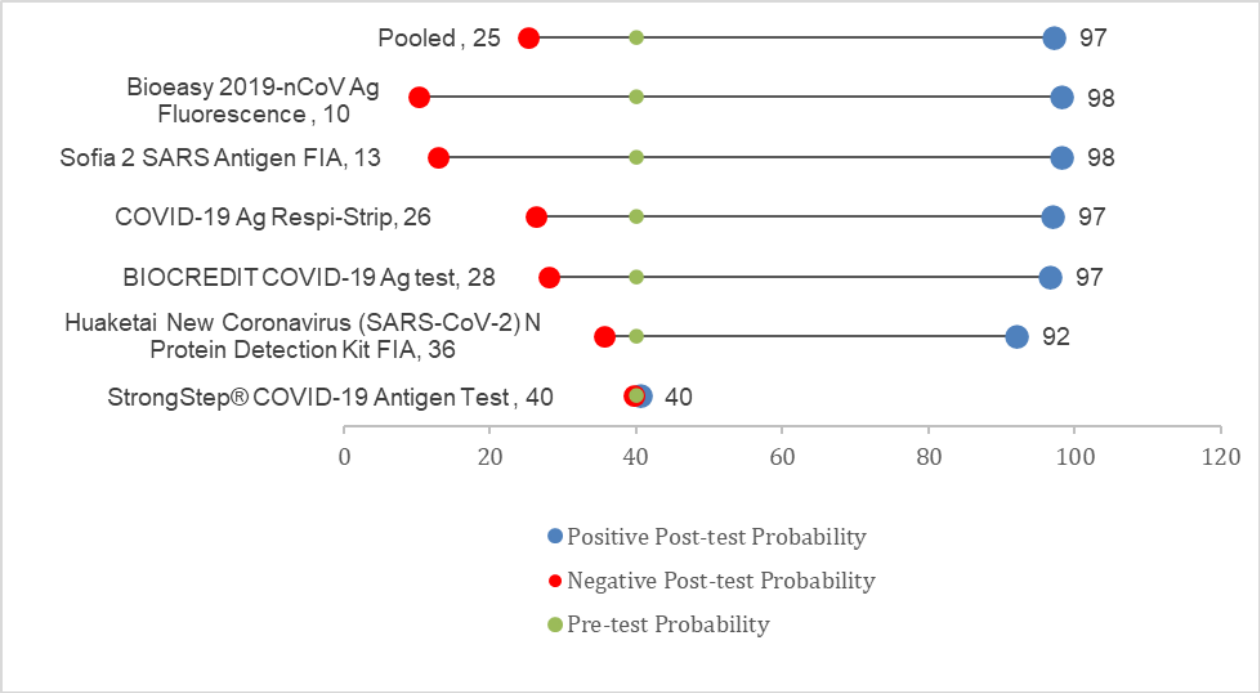

Figure 10. Dumbbell plot showing the post-test probabilities among symptomatic patients in hospital settings. Pretest probability was assumed to be 40%.

Recommendations from other guidelines

WHO does not recommend the use of rapid antigen tests for patient care and encourages more research on its clinical utility (WHO 2020). The US-NIH recommends the use of either molecular (e.g. RT-PCR) or antigen test in the diagnosis of COVID-19 in patients who present with COVID-19 like syndrome. However, an initial negative result in patients highly suspected with COVID-19 may warrant a confirmation with a molecular test (COVID-19 Treatment Guidelines Panel, 2020).

Conclusions

Based on moderate quality evidence, the use of rapid antigen tests as a screening tool for COVID-19 is limited by its low sensitivity. Rapid antigen tests have high specificity of 99% but a low sensitivity of 49%. Sensitivity estimates ranged from 0-94% in different studies and may have been affected by the study design, brand used, population tested, reference standard and type of specimen used, and day of illness when the test was done.

Implications for practice

Because of its high specificity, RAgT can be used to rule in the disease at a faster turnaround time. Interventions and management decisions (e.g., where to admit the patient) can be made at a faster rate compared to waiting for the RT-PCR results. In addition, it can allow faster tracing of contacts of positive cases.

However, because of its overall low sensitivity and the high uncertainty on its accuracy, we do NOT recommend these tests for screening asymptomatic disease (e.g., mass screening, contact

tracing, or return to work clearance). It may have some use for diagnosis confirmation when RT-PCR is not available or in patients with high pre-test probability such as suspected cases who are confined.

A negative result would still require confirmation with RT-PCR due to high false negative rate of RAgT. Negative results also need to be correlated with clinical (symptoms) and epidemiological parameters (exposure history).

Implications for research

More high quality prospective clinical validation studies of the RAgTs are needed before government agencies invest in these tests. The studies should include asymptomatic individuals, testing individuals beyond the first week of symptom onset, ensuring blinded analyses of both RT-PCR and RAgT, and interpreting RAgT results within hours from specimen collection.

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Declarations of interest

Howell Henrian G Bayona: none known
Ian Theodore G Cabaluna: none known
Leonila F Dans: none known
Antonio P Dans: none known

Table 1. Summary of study characteristics

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
Included studies							
Diao, 2020	China	Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit	nasopharyngeal swab	Symptomatic	239	ABI Prism 7500, Light Cycler 480 real-time PCR	Nasopharyngeal swab
Herrera, 2020	USA	Sofia 2 SARS Antigen FIA	nasopharyngeal swab	Symptomatic	1172	RT-PCR (not specified)	Not specified
Lambert-Niclot, 2020	France	COVID-19 Ag Respi-Strip	nasopharyngeal swab	Not reported	138	1. RealStar (Altona Diagnostics) 2. Bosphore novel coronavirus detection kit (Anatolia Geneworks) 3. Cobas 6800 (Roche) 4. All-plex 2019 novel CoV assage (Seegene)	Nasopharyngeal swab
Mak, 2020	Hong Kong	BIOCREDIT COVID-19 Ag test	Throat saliva (n = 122) Nasopharyngeal swab and throat swab (n = 103) Nasopharyngeal aspirate and throat swab (n = 81) Sputum (n = 62)	Positive SARS-CoV-2 samples; no information regarding patient characteristics	160	NxtScript Enzyme and Master Mix, Roche Diagnostis GmbH, Germany)	Throat saliva (n = 122) Nasopharyngeal swab and throat swab (n = 103) Nasopharyngeal aspirate and throat swab (n = 81) Sputum (n = 62)
Mertens, 2020	Belgium	COVID-19 Ag Respi-Strip	nasopharyngeal swab (n = 322) nasopharyngeal aspirate (n = 4) bronchoalveolar lavage (n = 2)	Symptomatic patients (n = 328) and healthcare workers (n = 53)	328	1. Taqman Fast Virus 1-Step Master Mix (Thermo Fisher) 2. Panther Fusion (PF, Hologic, San Diego, USA) Open AccessTM SARS-CoV analysis	nasopharyngeal swab (n = 322) nasopharyngeal aspirate (n = 4) bronchoalveolar lavage (n = 2)

Nagura-Ikeda, 2020	Japan	ESPLINE® SARS-CoV-2	Saliva	Symptomatic (n = 88, 85%); mild (n = 72, 82%), severe (n = 16, 18%) Asymptomatic (n = 15, 15%) 64.1% males, median age 45 (IQR 38-63, range: 18-87) Median time from onset of symptoms to specimen collection = 7 days (IQR 6-10; range: 1-14 days) - Early phase (≤ 9 days) = 61 patients - Late phase (> 9 days) = 27 patients	103	1. SARS-CoV-2 Direct Detection RT-qPCR Kit (Takara Bio Inc. Kusatsu, Japan) 2. AmpdirectTM 2019 Novel Coronavirus Detection Kit (Shimadzu Corporation, Kyoto, Japan) 3. Same primer sets as used in the LDT RT-qPCR method	Nasopharyngeal swab Oropharyngeal swab
Porte, 2020	Chile	Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit	nasopharyngeal swab and oropharyngeal swab	Symptomatic 53.5% males, median age 38 years Patients with respiratory symptoms and/or fever and an epidemiological risk factor for SARS-COV-2 infection Median time of symptom duration before testing date = 2 days (IQR 1-4); 118/126 (94%) tested within first week of symptoms (0-7 days)	127	Genesig® Real-Time PCR assay (Primerdesign Ltd., Chander´s Ford, UK)	Nasopharyngeal swab Oropharyngeal swab
Scohy, 2020	Belgium	COVID-19 Ag Respi-Strip	nasopharyngeal swab	Symptomatic (n = 86, 58%) Asymptomatic (n = 45, 30%)	148	Genesig® Real-Time PCR assay (Primerdesign Ltd., Chander´s Ford, UK)	Nasopharyngeal swab

				Unknown (n = 17, 11%) 64 men, 84 women; median age 57.5 years (range: 0-94) Median time of symptom duration before testing date = 4 days (range: 0-34)			
Weitzel, 2020	Chile	BIOCREDIT COVID-19 Ag test	nasopharyngeal swab and oropharyngeal swab	Symptomatic only 45% males, median age 40 years Median time of symptom duration before testing date = 2 days (IQR 1-5); 88% tested within first week of symptoms	348	Genesig® Real-Time PCR assay (Primerdesign Ltd., Chander´s Ford, UK)	Nasopharyngeal swab
Excluded studies							
Blairon, 2020	Belgium	COVID-19 Ag Respi-Strip	nasopharyngeal swab	Not reported	774	qRT-PCR (not specified)	Nasopharyngeal swab

Table 2. Diagnostic accuracy of RAgTs in included studies.

Study ID	N	Sensitivity		Specificity		Positive Predictive Value		Negative Predictive Value		Diagnostic Accuracy		Positive Likelihood Ratio		Negative Likelihood Ratio	
		%	95%CI	%	95%CI	%	95%CI	%	95%CI	%	95%CI	LR+	95% CI	LR-	95% CI
Diao, 2020[1]	239	67.8	61.2, 73.8	100	88.9, 100	100	97.4, 100	31.6	23.3, 41.4	72.0	66.0, 77.3	21.7	3.0, 155	0.32	0.31, 0.33
Herrera, 2020[7]	1172	76.7	72.6, 80.3	99.2	98.2, 99.6	98.3	96.4,99.2	86.9	84.3, 89.0	90.4	88.5, 91.9	91.1	65.6, 127	0.24	0.23, 0.24
Lambert-Niclot, 2020[3]	138	50	40.1, 59.9	100	92.0, 100	100	92.4, 100	48.4	38.4, 58.5	65.9	57.7, 73.3	22.5	3.0, 167	0.5	0.48, 0.52
Mak, 2020[2]	173	31.9	25.2, 39.5	-	-	100	93.0, 100	-	-	31.9	25.2, 39.5	-	-	-	-
Mertens, 2020[3]	328	57.6	49.1, 65.7	99.5	97.2, 99.9	98.7	93.0, 99.8	77.7	72.1, 82.4	82.6	78.2, 86.3	113	15.6, 817	0.43	0.41, 0.44
Nagura-Ikeda, 2020[4]	103	11.7	6.8, 19.3	-	-	100	75.8, 100	-	-	11.7	6.8, 19.3	-	-	-	-
Porte, 2020[1]	127	93.9	86.5, 97.4	100	92.1, 100	100	95.3, 100	90	78.6, 95.7	96.1	91.1, 98.3	43.2	6.1, 307	0.06	0.04,0.09
Scohy, 2020[3]	148	30.2	22.3, 39.5	100	91.6, 100	100	89.3, 100	36.21	28.0, 45.3	50	42.1, 58.0	13.0	1.59, 106	0.69	0.68, 0.72
Wietzel, 2020(A)[2]	109	62	51.0, 71.9	100	88.7, 100	100	92.7, 100	50	37.7, 62.3	72.5	63.4, 80	19.2	2.64, 134	0.38	0.36, 0.41
Wietzel, 2020(B)[5]	19	0	0, 29.9	90.0	59.6, 98.2	0	0, 79.4	50	29.0, 71.0	47.4	27.3, 68.3	0	-	1.11	0.78,1.26
Wietzel, 2020(C)[6]	109	16.7	10.0, 26.5	100	89.0, 100	100	77.2, 100	32.3	23.8, 42.2	40.4	31.6, 49.8	5.33	0.35,80.5	0.83	0.81, 0.86
Wietzel, 2020(D)[1]	111	85	75.6, 91.2	100	89.0, 100	100	94.7, 100	72.1	57.3, 83.3	89.2	82.1, 93.7	27.2	3.8,194	0.15	0.13, 0.18

Rapid antigen test brands used in each study are listed below:

[1] Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit (China)

[2] BIOCREDIT COVID-19 Ag test (Korea)

[3] COVID-19 Ag Respi-Strip (Belgium)

[4] ESPLINE® SARS-CoV-2 (Japan)

[5] StrongStep® COVID-19 Antigen Test (China)

[6] Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit FIA (China)

[7] Sofia 2 SARS Antigen FIA (USA)

Table 3. Results of investigations of heterogeneity (Subgroup analysis).

Covariate	Studies		Participants	Sensitivity		Specificity	
Test brand	**n**	**Study ID**	**n**	**%**	**95% CI**	**%**	**95% CI**
Bioeasy 2019-nCoV Ag Fluorescence (Shenzhen Bioeasy Biotechnology Co., Ltd, Shenzen, China)	3	Diao 2020 Porte 2020 Weitzel 2020	477	82.3	66.0, 98.5	100	97.1, 102.9
Sofia 2 SARS Antigen FIA (Quidel Corporation, USA)	1	Herrera, 2020	1172	76.7	72.6, 80.3	99.2	98.2, 99.6
COVID-19 Ag Respi-Strip (Coris Bioconcept, Gembloux, Belgium)	3	Lambert-Niclot 2020 Mertens 2020 Scohy 2020	614	45.9	29.2, 62.6	99.5	98.6, 100.5
BIOCREDIT COVID-19 Ag test (RapiGEN, Inc., Gyeonggi-do, South Korea)	2	Mak 2020 Weitzel 2020	269	41.3	35.3, 47.3	100	88.6, 100
Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit FIA (Savant Biotechnology Co., Beijing, China)	1	Weitzel 2020	109	16.7	10.0, 26.5	100	89.0, 100
ESPLINE® SARS-CoV-2 (Fuji Rebio Inc., Tokyo, Japan)	1	Weitzel 2020	103	11.7	6.8, 19.3	-	NA
StrongStep® COVID-19 Antigen Test (Liming Bio-Products, China)	1	Weitzel 2020	19	0	0, 29.9	100	72.2, 100
Presence of symptoms	**n**	**Studies**	**Participants**	**%**	**95% CI**	**%**	**95% CI**
Symptomatic	7	Diao 2020 Herrera 2020 Mertens 2020 Nagura-Ikeda 2020 Porte 2020 Scohy 2020 Weitzel 2020	2388	50.3	20.0, 80.7	99.6	98.8, 100.5
Asymptomatic	2	Nagura-Ikeda 2020 Scohy 2020	60	18.6	4.7, 32.5	100	89.0, 100
Undefined	2	Lambert-Niclot 2020 Mak 2020	298	38.0	32.1, 43.9	100	92.0, 100
Phase of disease	**n**	**Studies**	**Participants**	**%**	**95% CI**	**%**	**95% CI**
Early (0-7 days)	5	Nagura-Ikeda 2020 Herrera 2020	675	43.1	6.3, 79.8	100	97.7, 102.3

		Porte 2020 Scohy 2020 Weitzel 2020					
Late (8-14 days)	2	Nagura-Ikeda 2020 Porte 2020	35	12.7	3.2, 22.3	100	43.9, 100
Undefined	4	Diao 2020 Lambert-Niclot 2020 Mak 2020 Mertens 2020	2307	51.8	35.0, 68.7	99.3	98.7, 99.8
Type of specimen used	**n**	**Studies**	**Participants**	**%**	**95% CI**	**%**	**95% CI**
Nasopharyngeal swab	5	Diao 2020 Herrera 2020 Lambert-Niclot 2020 Mertens 2020[1] Scohy 2020	2025	56.7	40.8, 72.7	99.3	98.7, 99.8
Nasopharyngeal and oropharyngeal swab	3	Mak 2020 Scohy 2020 Weitzel 2020	510	50.5	6.4, 94.7	100	97.4, 102.6
Nasopharyngeal aspirate and throat swab	1	Mak 2020	35	34.3	20.8, 50.8	NA	NA
Saliva	2	Mak 2020 Nagura-Ikeda 2020	148	16.1	10.4, 21.8	NA	NA
Sputum	1	Mak 2020	45	11	4, 24	NA	NA

Table 4. Characteristics of ongoing/planned studies

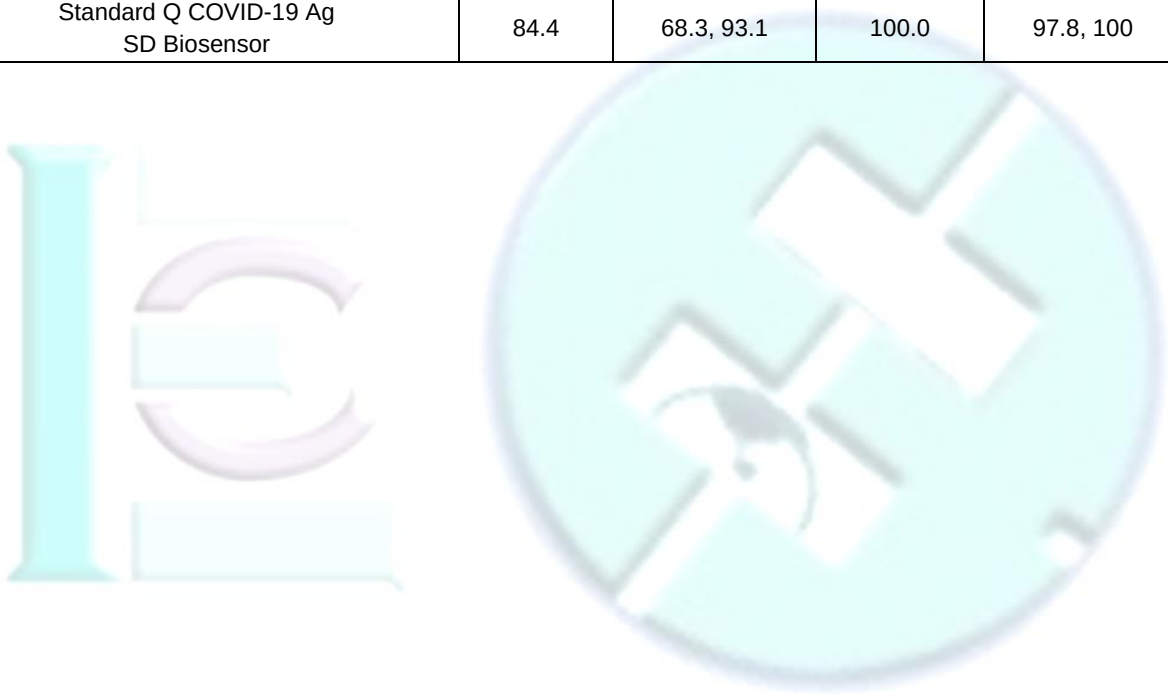
Clinical Trial ID	Title	Country	Antigen Test	Study design	Eligible Participants	Primary Outcome
CTRI/2020/07/026369	Evaluation of the performance of rapid diagnostic kit (COVIDAG-SP) in the detection of COVID-19 virus antigen	India	India Health Foundation-IHFs COVIDAG-SP	Observational Cross-sectional Multi-center	1. 18 years and above 2. Both males and females 3. Confirmed COVID-19 positive through RT-PCR in less than 24 hours of confirmation or Symptomatic and seeking RT-PCR testing to learn their COVID-19 status	1. Sensitivity, specificity of COVIDAG-SP using RT-PCR as reference standard 2. Sensitivity, specificity of nasopharyngeal swab, saliva, serum sample for scFv antigenic marker
UMIN000040386	Evaluation of COVID-19 antigen test in COVID-19 suspected cases	Japan	Not specified	Observational	1. COVID-19 suspected patient 2. Patient who was performed genetic test 3. Patient who was obtained blood sample	Sensitivity, specificity, PPV, and NPV of COVID-19 antibody test in comparison with genetic test
DRKS00021220	Evaluation of the performance of novel rapid diagnostics for COVID-19 at point-of-care	Germany	1. Bioeasy (Guangdong Province, China) 2. SD BIOSENSOR (Suwon, South Korea) 3. Other antigen tests	Observational Cross-sectional Single-center	1. Any gender 2. 18 years and above 3. Suspected COVID-19 cases; preselected by local Public Health Department	1. Sensitivity and specificity using RT-PCR as reference standard 2. Time to proficiency, implementation issues, design related issues at POC 3. Survival analysis for the outcome of death within 2-3 months by COVID and Antigen test status
NCT04403906	Somerset and South Essex Coronavirus Antigen Testing (SOCRATES)	United Kingdom	PCL COV05 - COVID 19 Ag Rapid FIA test (Seoul, South Korea)	Observational Cross-sectional Multi-center	1. Participant has clinical indication for a COVID diagnostic test and a clinical blood sample from which whole blood or plasma will be leftover for storage 2. 18 years and older 3. Any gender	1. Sensitivity and specificity of the rapid antigen testing to current PCR test and any future developed reference test (within 24 hrs) 2. Number of technically failed samples due to test issues (within 30 minutes) 3. Time taken for PCL Antigen test result (within 30 minutes)

NCT04348864	Assessment of COVID-19 IgM/IgG Self-testing Using Virtual Point-of-care	USA	Not specified	Interventional (Non-randomized clinical trial) Double-arm	1. Any gender 2. 18 years and older 3. Individuals who have experienced symptoms of COVID-19 and have been tested using a CDC approved or FDA registered and listed nucleic acid based test within 1 year of Feb 1, 2020. 4. Individuals who are at the time of enrollment in the study currently or in the recent past (3 weeks) exhibiting symptoms of COVID-19. 5. Individuals capable of performing a finger stick blood drop draw and placing it on the sample well. 6. Individuals that have interacted with a COVID-19 positive individual and are still exhibiting symptoms will be tested by the Colorado Department of Public Health with a CDC approved or FDA registered nucleic acid based device. 7. Individuals must be capable of navigating a mobile device to take an image of the test using the camera and enter information into fields on the device and wireless/cellular capability to upload one or more images to a website server.	1. Clinical accuracy of the antibody and antigen rapid tests compared to LAMP/PCR-based test result (1 year) 2. Clinical accuracy of the antibody and antigen rapid tests based on Clinical diagnosis (1 year) 3. Clinical accuracy of the subject's visual interpretation of the test result vs image analysis from clinician (1 year) 4. Ease of self-testing procedure (1 year)
NCT04337996	Dynamic Evaluation of COVID-19 Diagnostic Tests (TRODVID-19)	France	Not specified	Interventional (Non-randomized clinical trial) Single-arm	1. Symptomatic patient with confirmed Gold-Standard SARS-CoV-2 (COVID-19) infection 2. Presenting at least one criterion for hospitalization: - Respiratory failure and oxygenation - Circulatory failure (systolic BP < 90 mmHg) - Neurological failure (confusion, drowsiness, altered consciousness) - Polypathological terrain and co-morbidities (chronic respiratory failure, heart failure or cardiovascular pathology, renal failure, diabetes, immunosuppression, obesity, cirrhosis) 3. Eligible for different sampling methods 4. Beneficiary of a social insurance scheme or entitled person 5. 18 years and older 6. All gender	1. Comparison of the Gold-Standard PCR, anamnesis, thoracic CT scan versus SARS-Cov-2 antigen, anamnesis and thoracic CT scan (within 24 hrs) 2. medical-economic comparison of the first-line use of the antigenic test

NCT04405492	Evaluation of Rapid Diagnostic Solutions, Serological and Molecular Tests for COVID-19 (ERap-COV)	France	Not specified	Intereventional (Clinical Trial) Single-arm	1. 18 years and older 2. All gender 3. Patients presenting for hospital admission on suspicion of SARS-Cov-2 infection based on the WHO definition and local guidelines 4. Patient or relative/trusted person who has been informed about the study and has given informed consent. 5. Caregivers exposed to COVID-19 in the course of their duties in the clinical departments of the Bicêtre and Paul Brousse hospitals. 6. Caregivers who gave informed consent 7. Clients presenting themselves in one of the volunteer dispensary pharmacies located in the Île-de-France region, who will be called "lay users".	1. Sensitivity and specificity of different tests (antigenic rapid tests, molecular tests, proteomic tests) compared to RT-PCR (Ct) in salivary samples and nasopharyngeal swabs 2. Sensitivity and specificity of immunological, antigenic, molecular and proteomic tests according to symptom duration, stage of the disease 3. Description of the incidence of infection among hospital caregivers, time to seroconversion according to clinical form, medium-term antibody persistence 4. Sensitivity and specificity of antigenic rapid tests, molecular tests, proteomic tests according to the sample used (salivary samples or nasopharyngeal swabs) and according to the duration of the symptoms 5. Suitability of rapid tests in view of its intended purpose for self-testing

Table 5. Diagnostic accuracy of rapid antigen tests based on data from package inserts.

Test brand	Sensitivity	95% CI	Specificity	95%CI
AFIAS COVID-19 Ag Boditech Med Incorporated	87.5	69, 96	96.5	88.1, 99.0
BIOCREDIT COVID-19 Ag Rapigen	92.0	75, 97.8	98.0	89.5, 99.7
Kewei COVID-19 Antigen Rapid Assay Beijing Kewei Clinical Diagnostic Reagent Inc.	85.0	64, 94.8	100.0	96.3, 100
FaStep COVID-19 Antigen Rapid Test Device Assure Tech. (Hangzhou) Co. Ltd.	80.2	73.9, 85.3	100.0	97.7, 100
ichroma™ COVID-19 Ag Boditech Med Incorporated	87.5	69, 95.6	94.7	88.1, 99.0
Sofia SARS Antigen FIA Assay Quidel Corporation	87.5	52.9, 97.8	100.0	96.9, 100
Standard Q COVID-19 Ag SD Biosensor	84.4	68.3, 93.1	100.0	97.8, 100



Appendix

SEARCH STRATEGY (15 August 2020 5:27 PM)

#	Query	Results
1	("Coronavirus Infections"[Mesh] OR novel coronavirus OR NCOV OR "COVID-19"[Supplementary Concept] OR covid19 OR covid 19 OR covid-19 OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR severe acute respiratory syndrome coronavirus 2 OR SARS2 OR SARS 2 OR SARS COV2 OR SARS COV 2 OR SARS-COV-2)	52,699
2	"COVID-19 Ag Respi-Strip" OR "BIOCREDIT COVID-19 Ag" OR "STANDARD F COVID-19 Ag" OR "STANDARD Q COVID-19 Ag" OR "Bioeasy 2019-nCoV Ag"	8
3	((rapid OR point-of-care OR "point of care" OR poc OR poct) n3 antigen)	185
4	(test OR tests OR detect* OR diagnos* OR kit OR kits OR assay*)	10,759,139
5	#3 and #4	153
6	rapid antigen test* OR "rapid antigen detection test" OR radt OR radts OR rdt OR rdts OR ragt OR (antigen* n3 detect*)	16,579
7	#5 OR #6	16,628
8	#7 OR #2	16,632
9	#1 and #8	**123**

CHARACTERISTICS OF STUDIES

Diao 2020

Study characteristics	
Patient sampling	Purpose: to evaluate the significance of a fluorescence immunochromatographic assay for detecting nucleocapsid protein of SARS-CoV-2 in nasopharyngeal swab samples and urine Design: prospective cohort (clinical trial) Participant recruitment method: consecutive enrollment Number of patients/samples: 239 Inclusion criteria: nasopharyngeal swab and urine samples from suspected cases of COVID-19 Exclusion criteria: contaminated, duplicate, or unclear samples; samples with

	missing information from the original records of clinical trials; samples conditions do not meet the program requirements.
Patient characteristics and setting	Location: China, 7 hospitals Dates: not reported Symptoms and severity: symptomatic, severity not reported Demographics: suspected COVID-19 cases Exposure history: not reported Onset of symptoms: not reported
Index tests	Name/Brand: Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit Manufacturer: Shenzhen Bioeasy Biotechnology Co., Ltd, Shenzen, China Test use case: alone Index test specimen: nasopharyngeal swab OR urine Target antigen: nucleocapsid protein Blinding: blinded to RT-PCR results Interpretation: manufacturer standards; automated/reader; pre-determined by obtaining mean value from 100 healthy people plus 5 SD)
Reference standards	Target condition: SARS-CoV-2 infection Reference standard: RT-PCR (ABI Prism 7500, Light Cycler 480 real-time PCR) Target antigen: SARS-CoV-2 ORFlab and N gene region Specimen used: nasopharyngeal swab Blinding and interpretation: blinded to antigen test results; interpreted according to manufacturer instructions Timing of test: parallel with antigen testing
Flow and timing	<24 hrs (both tests done in parallel)

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
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			
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?	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?	Yes		
Could the patient flow have introduced bias?		Low risk	

Herrera 2020

Study characteristics	
Patient sampling	Purpose: internal validation of SARS-CoV-2 antigen testing Design: cohort Participant recruitment method: not specified Number of patients/samples: 1172 Inclusion criteria: not specified Exclusion criteria: not specified
Patient characteristics and setting	Location: Orlando, Florida, USA (AdventHealth) Dates: not stated Symptoms and severity: symptomatic and asymptomatic Demographics: not specified Exposure history: not specified Onset of symptoms: not specified

Index tests	Name/Brand: Sofia 2 SARS Antigen FIA Manufacturer: Quidel Corporation, California, USA Test use case: alone Index test specimen: nasopharyngeal swab Target antigen: nucleocapsid protein Blinding: unknown Threshold: manufacturer standards Interpretation: automated/reader
Reference standards	Target condition: SARS-CoV-2 infection Reference standard: RT-PCR Target antigen: not reported Specimen used: not reported Blinding and interpretation: not reported Timing of test: not reported
Flow and timing	Time interval: not reported Excluded patients: none

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
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			
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?	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?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Unclear risk	

Lambert-Niclot 2020

Study characteristics	
Patient sampling	Purpose: to evaluate a rapid diagnostic test, COVID-19 Ag Respi-Strip (Coris Bio-Concept, Gembloux, Belgium), for detection of the SARS-CoV-2 antigen in nasopharyngeal secretions Design: cross-sectional Participant recruitment method: not specified (laboratory-based) Number of patients/samples: 138 Inclusion criteria: not specified Exclusion criteria: samples collected in cobas medium (n = 4)
Patient characteristics and setting	Location: France (Assistance-Publique-Hôpitaux de Paris (APHP)) Dates: 01 Apr 2020 - 15 Apr 2020 Symptoms and severity: not specified Demographics: not specified Exposure history: not specified Onset of symptoms: not specified
Index tests	Name/Brand: COVID-19 Ag Respi-Strip Manufacturer: Coris Bioconcept, Gembloux, Belgium Test use case: alone Index test specimen: nasopharyngeal swab Target antigen: nucleocapsid protein Blinding: not reported Interpretation: manufacturer standards; visual readout

Reference standards	Target condition: SARS-CoV-2 infection Reference standard: RT-PCR 1. RealStar (Altona Diagnostics) 2. Bosphore novel coronavirus detection kit (Anatolia Geneworks) 3. Cobas 6800 (Roche) 4. All-plex 2019 novel CoV assage (Seegene) Target antigen: SARS-CoV-2 E gene Specimen used: nasopharyngeal Blinding and interpretation: not reported
Flow and timing	<24 hrs (no cooling or freezing step)

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
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 concern
DOMAIN 2: Index Test			
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?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

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?	Yes		
Could the patient flow have introduced bias?		Low risk	

Mak 2020

Study characteristics	
Patient sampling	Purpose: to assess the diagnostic use of BIOCREDIT COVID-19 Ag test -- (1) assess the limit of detection (LOD), (2) evaluate diagnostic performance of RAD test in detecting SARS-CoV-2 in different types of respiratory samples Design: cohort Participant recruitment method: laboratory samples, all positive for SARS-CoV-2 Number of patients/samples: 160 respiratory samples from 152 patients (from total of 368 available samples), divided into different specimens: (a) throat saliva (n = 45) (b) nasopharyngeal swab + throat swab (NPS & TS, n = 35) (c) nasopharyngeal aspirate and throat swab (NPA & TS, n = 35) (d) sputum (n = 45) Inclusion criteria: not reported Exclusion criteria: not reported
Patient characteristics and setting	Location: Public Health Laboratory Services Branch (PHLSB), Hong Kong Date: 1 Feb 2020 - 21 Apr 2020 Symptoms and severity: not specified Demographics: not specified Exposure history: not specified
Index tests	Name/Brand: BIOCREDIT COVID-19 Ag Manufacturer: RapiGEN, Inc., Gyeonggi-do, South Korea Test use case: alone Index test specimen: NPS & TS, NPA & TS, sputum and throat saliva Target antigen: no information Blinding: none; only SARS-CoV-2 positive samples were tested using RAgT Interpretation: visual; all samples tested using modified sample processing methods by either eluting in VTM or suspending in PBS Tests were undertaken using procedures different from manufacturer's standards

Reference standards	Target condition: SARS-CoV-2 Reference standard: RT-PCR (NxtScript Enzyme and Master Mix, Roche Diagnostics GmbH, Germany) Target antigen: SARS-CoV-2 RdRp gene Specimen used: NPS & TS, NPA & TS, throat saliva, sputum Blinding and interpretation: all RT-PCR tests done before RAgTs
Flow and timing	Samples were refrigerated after completion of RT-PCR and only tested with RAgT after an unspecified period of time

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
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 concern
DOMAIN 2: Index Test			
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?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High 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?	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?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Mertens 2020

Study characteristics	
Patient sampling	Purpose: to describe the analytical performance of the COVID-19 Ag Respi-Strip; to reflect on the risk management and conditions to be fulfilled before implementation of point-of-care test outside the hospital Design: multi-center, retrospective Participant recruitment method: randomly selected samples Number of patients/samples: 328 samples Inclusion criteria: not specified Exclusion criteria: not specified
Patient characteristics and setting	Location: Brussels, Belgium Date: 19 Mar 2020 - 30 Mar 2020 Symptoms and severity: symptomatic Demographics: patients and healthcare workers suspected with COVID-19 Exposure history: not specified Majority of the patients were found to have high viral loads (Ct mean = 22.2)
Index tests	Name/Brand: COVID-19 Ag Respi-Strip Manufacturer: Coris Bioconcept, Inc., Gembloux, Belgium Test use case: alone Index test specimen: nasopharyngeal swab (n=322), nasopharyngeal aspirate (n=4), broncho-alveolar lavage (n=2) Target antigen: nucleocapsid protein Blinding: not reported Interpretation: visual; following manufacturer's instructions
Reference standards	Target condition: SARS-CoV-2 Reference standard: RT-PCR 1. Taqman Fast Virus 1-Step Master Mix (Thermo Fisher) 2. Panther Fusion (PF, Hologic, San Diego, USA) Open AccessTM SARS-CoV analysis Target antigen: SARS-CoV-2 E gene and RdRp gene Specimen used: nasopharyngeal swab (n=322), nasopharyngeal aspirate (n=4), broncho-alveolar lavage (n=2) Blinding and interpretation: Not reported
Flow and timing	RAgT testing was done on leftover sample material after qRT-PCR analysis

	with a delay of 1 hr to 2 days. Samples stored at 4◦C. Four clinical samples showed diminished intensity of reaction after 24h, suggesting possible effect of time delay

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
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			
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?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	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?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Nagura-Ikeda 2020

Study characteristics	
Patient sampling	Purpose: to describe the clinical performance of various molecular diagnostic methods including LDT RT-qPCR, cobas SARS-CoV-2 high-throughput system, direct RT-qPCR kits, and RT-LAMP, and a commercial SARS-CoV-2 RAgT on self-collected saliva specimens in diagnosing COVID-19. Participant recruitment method: consecutive enrollment Number of patients/samples: 103 Inclusion criteria: patients referred by hospital for isolation and treatment Exclusion criteria: not specified
Patient characteristics and setting	Location: Japan (Self-Defense Forces Central Hospital) Date: 11 Feb 2020 - 13 May 2020 Symptoms and severity: symptomatic and asymptomatic (patients referred for isolation and treatment by hospital, asymptomatic patients associated with family clusters or mass screening in an outbreak) Demographics: Age 18-87 years (median 46; IQR 38-63) Sex: males = 66 (64.1%) Clinical profile: - Symptomatic patients = 88 (85.4%); mild = 72 (81.8%), severe = 16 (18.2%) - Asymptomatic patients = 15 (14.5%) Onset of symptom: time from symptom onset to sample collection was 1–14 days (median, 7 d; IQR, 6–10 d) Exposure history: not specified
Index tests	Name/Brand: ESPLINE® SARS-CoV-2 Manufacturer: Fuji Rebio Inc., Tokyo, Japan Test use case: alone Index test specimen: saliva Target antigen: nucleocapsid protein Blinding: none; all samples tested for RAgT were RT-PCR positive Interpretation: visual; performed according to manufacturer's instructions
Reference standards	Target condition: SARS-CoV-2 infection Reference standard: RT-PCR 1. SARS-CoV-2 Direct Detection RT-qPCR Kit (Takara Bio Inc. Kusatsu, Japan) 2. AmpdirectTM 2019 Novel Coronavirus Detection Kit (Shimadzu Corporation, Kyoto, Japan) 3. same primer sets as used in the LDT RT-qPCR method Cycle threshold for positive samples: <40 (#1 and 2), <45 (#3)

	Target antigen: SARS-CoV-2 RdRp gene Specimen used: nasopharyngeal swab, oropharyngeal swab Blinding and interpretation: All RT-PCR tests were done before RAgTs
Flow and timing	Saliva specimens were collected from patients 3 days (median) after receiving their first positive RT-qPCR result.

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
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			
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 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		
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			Low concern

match the question?			
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		
Could the patient flow have introduced bias?		High risk	

Porte 2020

Study characteristics	
Patient sampling	Purpose: to evaluate a novel antigen-based RDT for the detection of SARS-CoV-2 in respiratory specimens from suspected Covid-19 cases Design: retrospective cohort Participant recruitment method: convenience sampling from a pool of 1,453 respiratory specimens processed for SARS-CoV-2 in the lab from March 16-21 2020 Number of patients/samples: 127 Inclusion criteria: patients with respiratory symptoms and/or fever, and with epidemiological risk factors (e.g., travel or contact with confirmed case) Exclusion criteria: not specified
Patient characteristics and setting	Location: Santiago, Chile (Clinica Alemana) Date: 16 March 2020 - 21 March 2020 Symptoms and severity: symptomatic (patients with fever and/or respiratory symptoms) Demographics: 53.5% male, median age 38 years Onset of symptom: median duration 2 days (IQR 1-4 days) from symptom onset to specimen collection; 118/126 (94%) of specimens taken during first week of symptoms Exposure history: not specified
Index tests	Name/Brand: Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit Manufacturer: Shenzhen Bioeasy Biotechnology Co., Ltd, Shenzen, China Test use case: alone Index test specimen: nasopharyngeal and oropharyngeal swab Target antigen: nucleocapsid protein Blinding: Same trained technician blinded to RT-PCR results Interpretation: reader; with approved deviation from manufacturer
Reference standards	Target condition: SARS-CoV-2 infection Reference standard: RT-PCR (Genesig® Real-Time PCR assay; Primerdesign Ltd, Chandler's Ford, UK) Cycle threshold for positive samples: <40 Target antigen: SARS-CoV-2 RdRp gene Specimen used: nasopharyngeal and oropharyngeal swab Blinding and interpretation: All RT-PCR tests done before RAgT
Flow and timing	All PCR samples were kept at 4C and tested with RAgT within 48 hours of RT-

	PCR

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
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			
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?	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?	Yes		
Could the patient flow have introduced bias?		Low risk	

Scohy 2020

Study characteristics	
Patient sampling	Purpose: to assess the performances of COVID-19 Ag Respi-Strip as a frontline testing in comparison to molecular technique Design: cross-sectional Participant recruitment method: random selection Number of patients/samples: 148 Inclusion criteria: not specified Exclusion criteria: not specified
Patient characteristics and setting	Location: Brussels, Belgium (Saint Luc Hospital) Date: 06 April 2020 - 21 April 2020 Symptoms and severity: not specified Demographics: not specified Exposure history: not specified
Index tests	Name/Brand: COVID-19 Ag Respi-Strip Manufacturer: Coris Bioconcept, Inc., Gembloux, Belgium Test use case: alone Index test specimen: nasopharyngeal swab (n=322), nasopharyngeal aspirate (n=4), broncho-alveolar lavage (n=2) Target antigen: nucleocapsid protein Blinding: not reported Interpretation: visual; following manufacturer's instructions
Reference standards	Target condition: SARS-CoV-2 infection Reference standard: RT-PCR (Genesig® Real-Time PCR assay; Primerdesign Ltd, Chandler's Ford, UK) Cycle threshold for positive samples: <40 Target antigen: SARS-CoV-2 RdRp gene Specimen used: nasopharyngeal swab Blinding and interpretation: Done according to manufacturer's instructions
Flow and timing	No information regarding how many samples were not tested on the same day. If the rapid antigen test was not performed immediately, samples were stored at 4 °C until the test.

Methodological quality			
Item	**Authors' judgment**	**Risk of bias**	**Applicability concerns**

DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
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			
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?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	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?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Weitzel 2020

Study characteristics	
Patient sampling	Purpose: to evaluate four novel antigen-based rapid diagnostic tests for the detection of SARS-CoV-2 in respiratory specimens from suspected COVID-19 cases Design: retrospective cohort Participant recruitment method: convenience sampling from 5,276 available respiratory specimens in the hospital Number of patients/samples: 111 (for each of the 4 RAgTs tested) Inclusion criteria: with respiratory symptoms and/or fever Exclusion criteria: not specified (both for patients and laboratory specimens)
Patient characteristics and setting	Location: Santiago, Chile (Clinica Alemana) Date: 16 March 2020 - 26 April 2020 Symptoms and severity: symptomatic (patients with fever and/or respiratory symptoms) Demographics: 55% female, median age 40 years Onset of symptom: median duration 2 days (IQR 1-5 days) from symptom onset to specimen collection; 88% of specimens taken during first week of symptoms Exposure history: not specified
Index tests	Name/Brand: 1. BIOCREDIT COVID-19 Ag 2. StrongStep® COVID-19 Antigen Test 3. Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit (FIA) 4. Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit Manufacturers: 1. RapiGEN, Inc., Gyeonggi-do, South Korea 2. Liming Bio-Products Co., Jiangsu, China 3. Savant Biotechnology Co., Beijing, China 4. Shenzhen Bioeasy Biotechnology Co., Ltd, Shenzen, China Test use case: alone Index test specimen: nasopharyngeal and oropharyngeal swab Target antigen: nucleocapsid protein Blinding: Same trained technician blinded to RT-PCR results Interpretation: visual (#1-3), reader (#4 - Bioeasy); deviated from manufacturers' instruction by using equivalent volume of UTM instead of the provided test solutions
Reference standards	Target condition: SARS-CoV-2 Reference standard: RT-PCR (Genesig® Real-Time PCR assay; Primerdesign Ltd., Chanders Ford, UK) Target antigen: SARS-CoV-2 E gene and RdRp gene Specimen used: naso-oropharyngeal swab Blinding and interpretation: RT-PCR was done before all RAgT testing
Flow and timing	Naso-oropharyngeal specimens were tested using RAgT on April 28 and 29, indicating a delay ranging from 2 to 44 days. All specimens kept at -80° C.

Methodological quality			
Item	**Authors'**	**Risk of bias**	**Applicability**

	judgment		concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
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			
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 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?	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?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

FOREST PLOTS

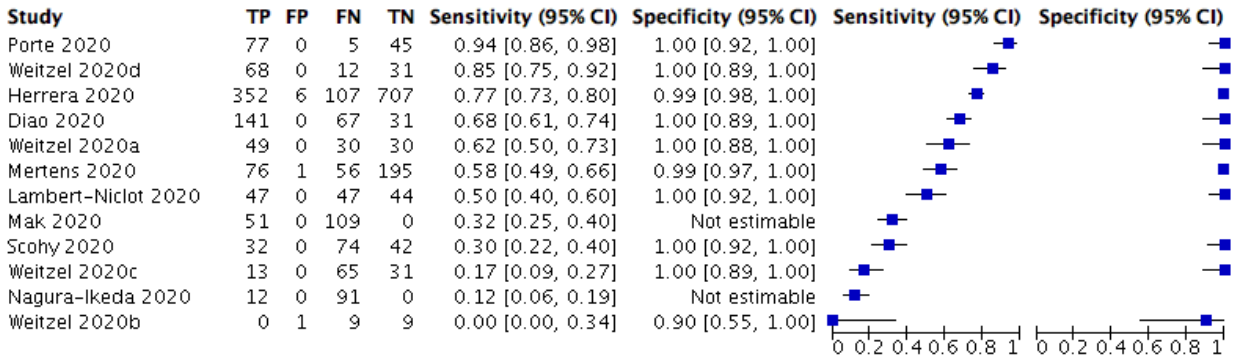


Figure 11. Forest plot of different rapid antigen tests across studies.

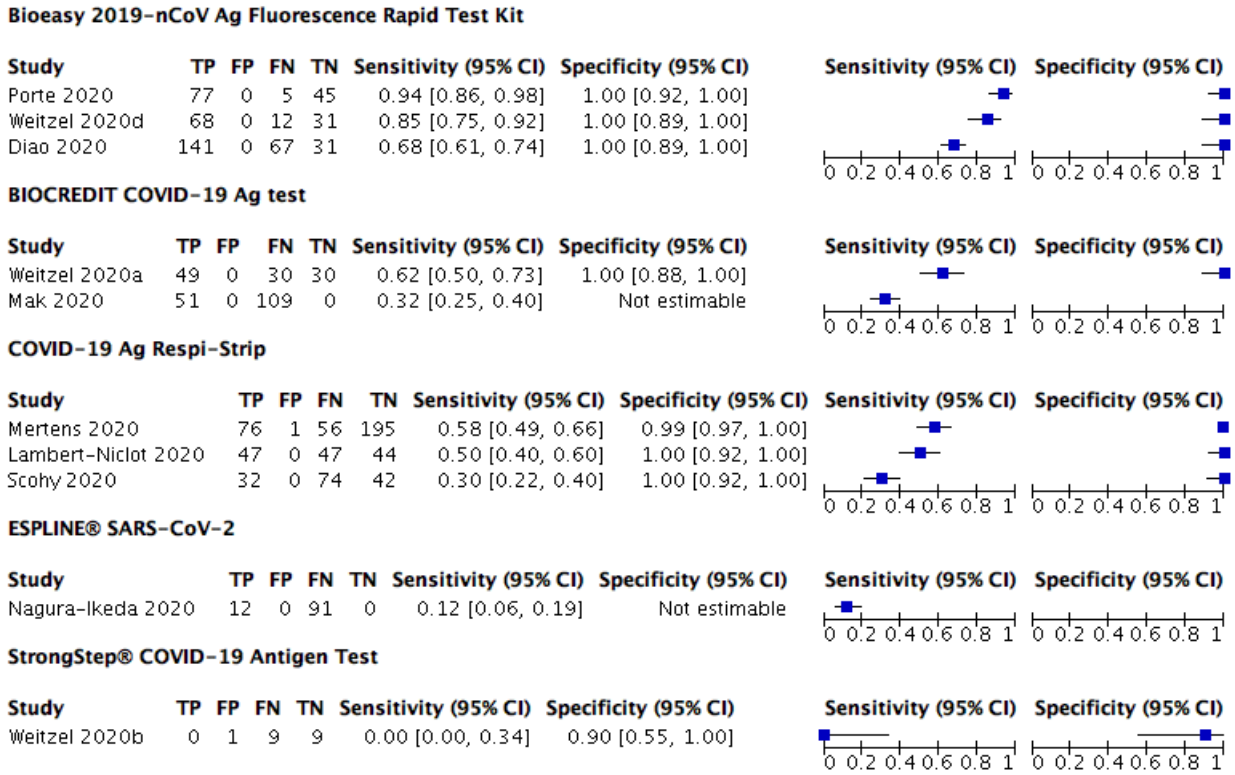


Figure 12. Forest plot of rapid antigen tests according to brand.

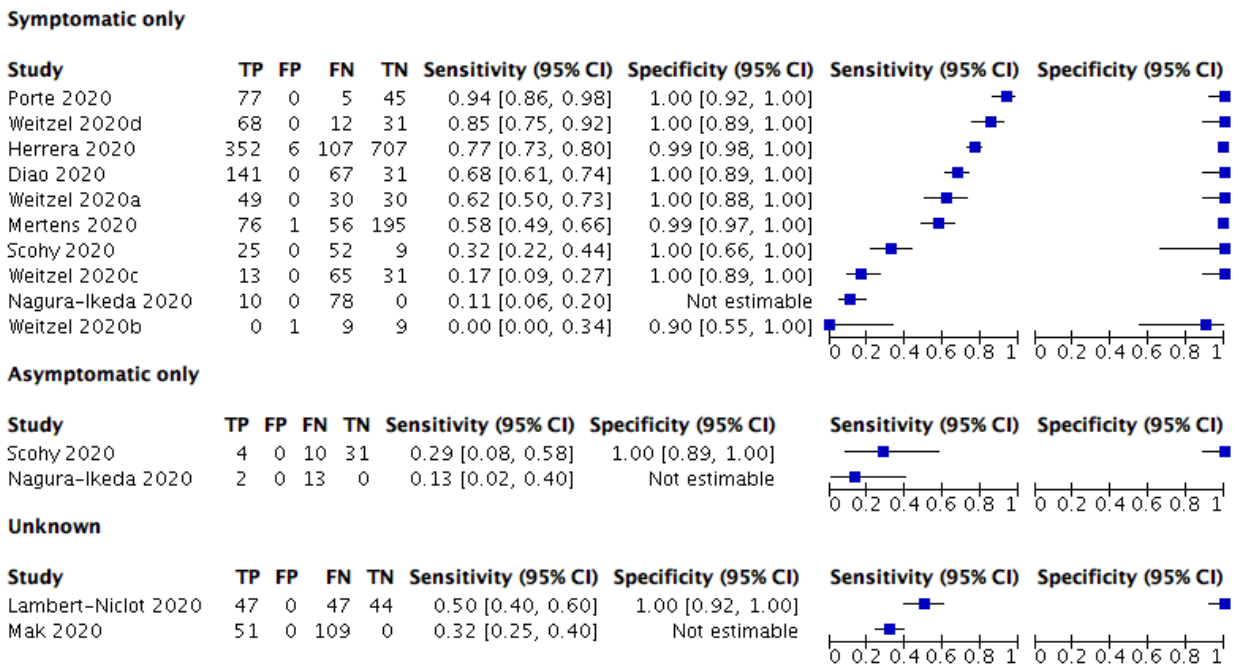


Figure 13. Forest plot of rapid antigen tests according to presence of symptoms.

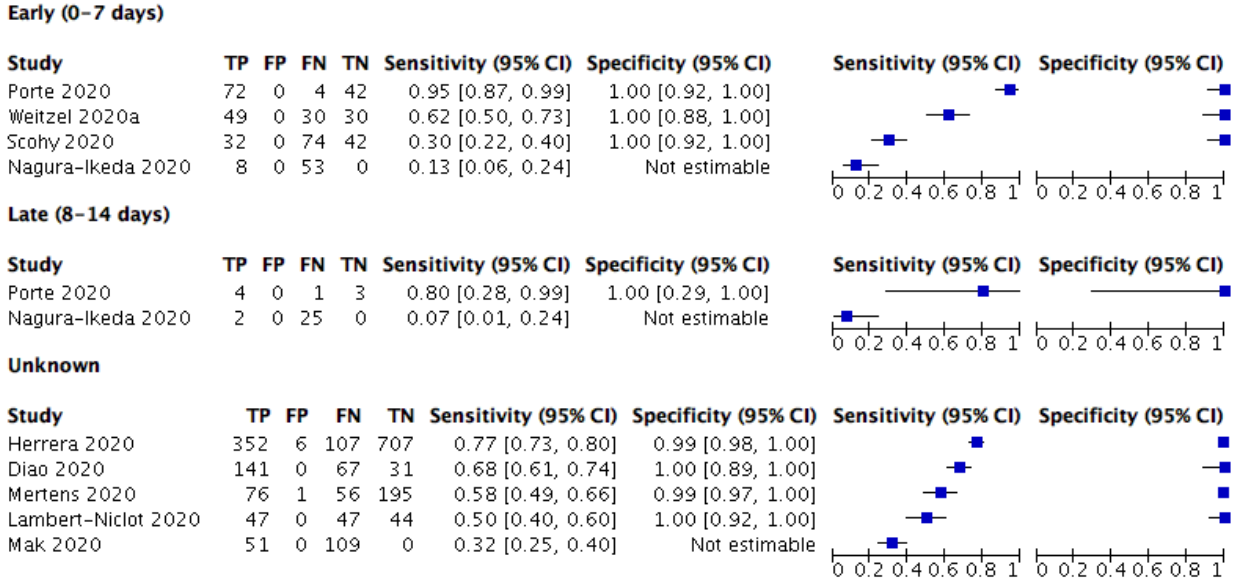


Figure 14. Forest plot of rapid antigen tests by phase of disease at time of testing: early (0-7 days), late (8-14 days), unknown.

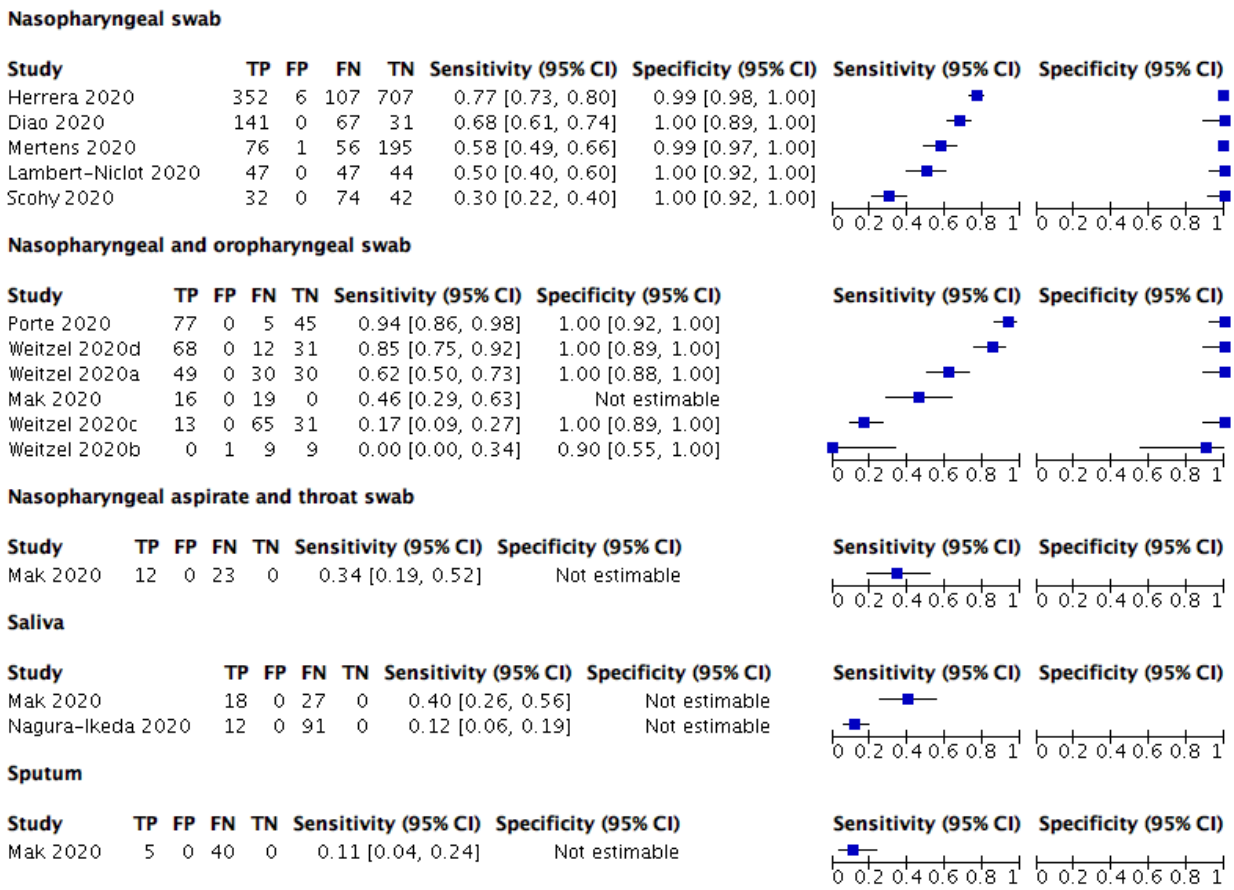
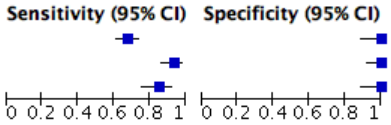


Figure 15. Forest plot of rapid antigen tests by type of specimen used.

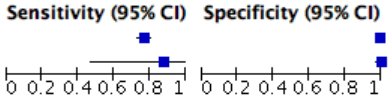
Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Diao 2020	141	0	67	31	0.68 [0.61, 0.74]	1.00 [0.89, 1.00]
Porte 2020	77	0	5	45	0.94 [0.86, 0.98]	1.00 [0.92, 1.00]
Weitzel 2020d	68	0	12	31	0.85 [0.75, 0.92]	1.00 [0.89, 1.00]



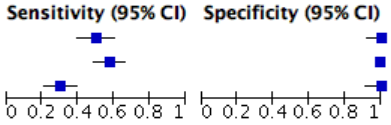
Sofia 2 SARS Antigen FIA

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Herrera 2020	352	6	107	707	0.77 [0.73, 0.80]	0.99 [0.98, 1.00]
Package Insert Data	7	0	1	118	0.88 [0.47, 1.00]	1.00 [0.97, 1.00]



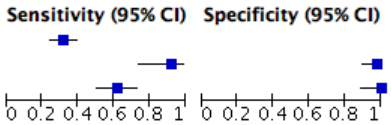
COVID-19 Ag Respi-Strip

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lambert-Niclot 2020	47	0	47	44	0.50 [0.40, 0.60]	1.00 [0.92, 1.00]
Mertens 2020	76	1	56	195	0.58 [0.49, 0.66]	0.99 [0.97, 1.00]
Scohy 2020	32	0	74	42	0.30 [0.22, 0.40]	1.00 [0.92, 1.00]



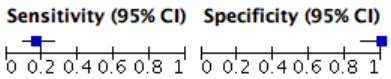
BIOCREDIT COVID-19 Ag test

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mak 2020	51	0	109	0	0.32 [0.25, 0.40]	Not estimable
Package Insert Data	23	1	2	49	0.92 [0.74, 0.99]	0.98 [0.89, 1.00]
Weitzel 2020a	49	0	30	30	0.62 [0.50, 0.73]	1.00 [0.88, 1.00]



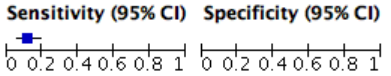
Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit FIA

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Weitzel 2020c	13	0	65	31	0.17 [0.09, 0.27]	1.00 [0.89, 1.00]



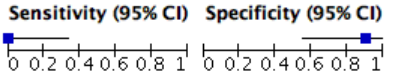
ESPLINE® SARS-CoV-2

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Nagura-Ikeda 2020	12	0	91	0	0.12 [0.06, 0.19]	Not estimable



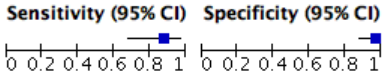
StrongStep® COVID-19 Antigen Test

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Weitzel 2020b	0	1	9	9	0.00 [0.00, 0.34]	0.90 [0.55, 1.00]



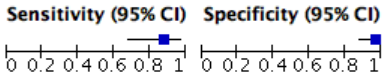
ichroma™ COVID-19 Ag

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Package Insert Data	21	2	3	55	0.88 [0.68, 0.97]	0.96 [0.88, 1.00]



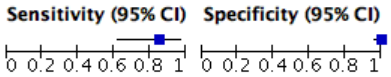
AFIAS COVID-19 Ag

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Package Insert Data	21	2	3	55	0.88 [0.68, 0.97]	0.96 [0.88, 1.00]



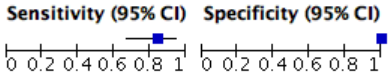
Kewei COVID-19 Antigen Rapid Assay

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Package Insert Data	17	0	3	100	0.85 [0.62, 0.97]	1.00 [0.96, 1.00]



Standard Q COVID-19 Ag

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Package Insert Data	27	0	5	170	0.84 [0.67, 0.95]	1.00 [0.98, 1.00]



FaStep COVID-19 Antigen Rapid Test Device

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Package Insert Data	150	0	37	161	0.80 [0.74, 0.86]	1.00 [0.98, 1.00]

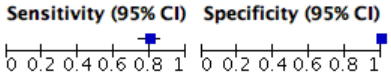


Figure 16. Forest plot of rapid antigen tests by brand, including data reported in package inserts.