Philippine COVID-19 Living Clinical Practice Guidelines
Institute of Clinical Epidemiology, National Institutes of Health, UP Manila
In cooperation with the Philippine Society for Microbiology and Infectious Diseases
Funded by the Department of Health

EVIDENCE SUMMARY

Among patients suspected to have COVID-19, how accurate are self-administered rapid antigen tests alone compared to RT-PCR for the diagnosis of COVID-19?

Review by: Giselle Anne Q. Adajar, MD, Marc Andrew O. Perez, MD, Michelle Cristine Miranda, MD, Howell Henrian G. Bayona, MSc, Marissa M. Alejandria, MD, MSc, Leonila F. Dans, MD, MSc

RECOMMENDATION

We suggest the use of self-administered rapid antigen test for the diagnosis of COVID-19 in symptomatic individuals, provided that ALL OF THE FOLLOWING conditions are met: *(Low certainty of evidence; Weak recommendation)*

1. Ease of collecting samples is ensured;
2. Ease of interpretation is ensured;
3. Test kits have passed flex studies; AND
4. Individuals present with symptoms for less than 7 days.

We suggest against the use of self-administered rapid antigen test for routine screening of COVID-19. *(Low certainty of evidence; Weak recommendation)*

Consensus Issues

The Panel unanimously agreed that all of the following four conditions should be met when using self-administered antigen tests for the diagnosis of COVID-19:

1. Ease of sample collection, because incorrect performance of self-administered tests largely affects diagnostic accuracy;
2. Ease of interpretation, because proper interpretation is important for the accurate clinical management of patients;
3. The test kits should have passed the flex studies, because the quality of the self-administered test kit should be ensured; and
4. Individuals present with symptoms for less than 7 days, because antigen tests perform best during this period; and beyond this, the use of the test is not cost-effective, thereby incurring costs without added benefit.

The panel decided on a weak recommendation based on evidence including seven observational studies where performance of self-testing by participants was supervised by trained personnel either onsite or via telehealth. None were conducted in a home setting. Additionally, the studies did not specify if the participants were close contacts of COVID-19 patients or if they have a high- or low-risk of contracting COVID-19.

Other issues raised include (1) the lack of locally FDA-approved self-administered antigen test kits, (2) differentiating antigen tests manufactured for self-administration versus those that are not (i.e., for trained personnel), (3) the method of reporting the test results, and (4) the subsequent management and/or protocols after a positive test result (e.g., contact tracing).

Key Findings

- Seven observational studies assessed the diagnostic accuracy of self-administered rapid antigen tests against RT-PCR as the reference standard. The studies included varied test brands (n=6), specimen types, and symptom status.
- The pooled sensitivity of self-administered rapid antigen test was moderate at 0.77 (95% CI 0.62-0.87) while the pooled specificity was high at 0.996 (95% CI 0.99-1.00). Pooled sensitivity estimates must be interpreted with caution due to the substantial heterogeneity (I^2=94%) across studies.
- On subgroup analysis, self-administered rapid antigen test showed higher sensitivity when used in the following conditions:
    - Symptomatic individuals (Sn 0.81, 95% CI 0.69-0.89);
    - Specimens taken from exhaled breath (Sn 0.92, 95% CI 0.64-1.0) or nasal mid-turbinate (Sn 0.81, 95% CI 0.73-0.87);
    - Specimens with high viral loads at RT-PCR cycle threshold <25 (Sn 0.87, 95% CI 0.68-0.88);
    - Specific brands of rapid antigen test, namely Inflammacheck device (Sn 0.92, 95% CI 0.64-1.0), Drager antigen test (Sn 0.89, 95% CI 0.79-0.95), and Abbott Panbio (Sn 0.84, 95% CI 0.71-0.94); and
    - Studies with high methodological quality or low risk of bias (Sn 0.79, 95% CI 0.68-0.86).
- The overall certainty of evidence for test sensitivity was low because of serious inconsistency (high heterogeneity) and risk of bias issues (patient selection, conduct of index test, and reference standard).

Introduction

Reverse-transcriptase polymerase chain reaction (RT-PCR) tests are considered the gold standard and the most sensitive option in the clinical diagnostic detection of SARS-CoV-2. However, RT-PCR-based assay is not entirely practical for all testing scenarios due to its need for additional specialized equipment, trained laboratory-based staff, and high cost. Recently, immunoassays such as rapid antigen tests (RAgTs) can detect the presence of specific viral antigens with a faster turnaround time, which may be performed at the point of care, and are relatively less expensive compared to RT-PCR tests.[1]

The review by Burog et al. in March 2021 showed that the pooled sensitivity and specificity of 30 studies and 10 evaluation reports on RAgTs were 72% (95% CI 64-78%, I^2=95.77) and 99% (95% CI 99-100%, I^2=93.16) respectively.[2] The pooled sensitivity of RAgTs were based on studies where testing was conducted by trained healthcare personnel. Only recently have studies evaluated the potential applicability of RAgTs among untrained users by way of self-administration.

Due to the ease of use of RAgTs, the use of self-administered RAgT or self-testing is being considered. As per World Health Organization (WHO) definition, self-testing involves either self-sampling, self-performance of testing, self-reading of test results, or all three. Self-administered RAgTs may potentially cut costs on personnel and equipment, with an added option of being done at the home setting.[1] Additionally, conventional nasopharyngeal swabs frequently induce pain and are perceived as uncomfortable and traumatizing.[3] However, the accuracy of self-testing or self-administration may be affected by incorrect performance of the user or patient. Hence, in this review, the existing evidence on the diagnostic accuracy of self-administered RAgTs in detecting SARS-CoV-2 will be evaluated.

Review Methods

A literature search was done using MEDLINE. Medical subject headings (MESH) combined with free text terms related to COVID-19 or SARS-CoV-2 and rapid antigen tests/testing were used, with no language limits or method filters.

Preprint studies were identified using the COVID-19 Living Evidence Database (https://zika.ispm.unibe.ch/assets/data/pub/search_beta/) with "antigen" as the search term. 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. Search for related links and journals was also carried out. Bibliography sections of the included studies were reviewed for relevant articles that might be missed by database search. The final search was done on September 14, 2021.

To supplement the initial search yield, available data on RAgT from FIND SARS-CoV-2 Diagnostic pipeline (https://www.finddx.org/covid-19/dx-data/) was retrieved. Relevant clinical trials were searched on clinicaltrials.gov. Local publications such as health technology assessments on the use of RAgTs were also sought. Methodological qualities of the diagnostic studies were assessed by independent reviewers using the QUADAS-2 instrument.

Heterogeneity was determined by visual inspection of the forest plots. Because of anticipated heterogeneity across studies, pooled sensitivity and specificity estimates were derived by stratifying studies according to test brand, type of specimen used, cycle threshold value used, and participant characteristics. Summary estimates were computed externally through a web-based app (MetaDTA v2.01; https://crsu.shinyapps.io/dta_ma/). Sensitivity analysis was performed by removing studies with low methodologic quality or with risk of bias issues in certain QUADAS-2 domains, and subsequently assessing their impact on overall diagnostic accuracy estimates.

A total of 475 titles and abstracts were screened, among which 192 full-text articles with correspondence to the key question were retrieved. Review of the retrieved articles yielded seven studies that specifically tackled the diagnostic accuracy of self-administered RAgTs.

Results

Characteristics of included studies

Seven observational studies including a total sample of 6,755 were found on self-administered antigen testing. Six different RAgT brands were evaluated using RT-PCR as the reference standard. All studies were done in a community setting. The studies used varied RAgT specimens: three used nasal mid-turbinate specimens [4-6], two used anterior nares specimens [7,8], one used combined nasal and oropharyngeal swabs [9], and one used exhaled breath condensates.[10] Three studies included only symptomatic patients [5,6,8], one included only asymptomatic patients [9], while three included both symptomatic and asymptomatic patients.[4,7,10] Only one study included children as participants, but the study did not provide sufficient data to allow subgroup analysis for this clinical population.[9] None of the studies were done at a home setting. All studies involved a personnel who supervised the participant at the study site. Appendix 3 shows a summary of the characteristics of included studies.

Methodological quality of included studies

The overall methodological quality of the included studies was rated as moderate. Two were rated as high quality [5,6] while five were of moderate quality [4,7-10] due to issues of unclear patient

selection, index test, and reference standard. Appendix 4 shows a detailed assessment of the risk of bias of included studies.

Diagnostic accuracy of self-administered RAgT

A. Overall diagnostic accuracy

Pooled analysis of the seven studies showed that self-administered RAgT had a moderate sensitivity at 0.77 (95% CI 0.62-0.87) with high heterogeneity (I^2=94%), and excellent specificity at 0.996 (95% CI 0.99-1.00). Figure 1 shows the forest plots of the pooled sensitivity and pooled specificity of self-administered RAgTs.

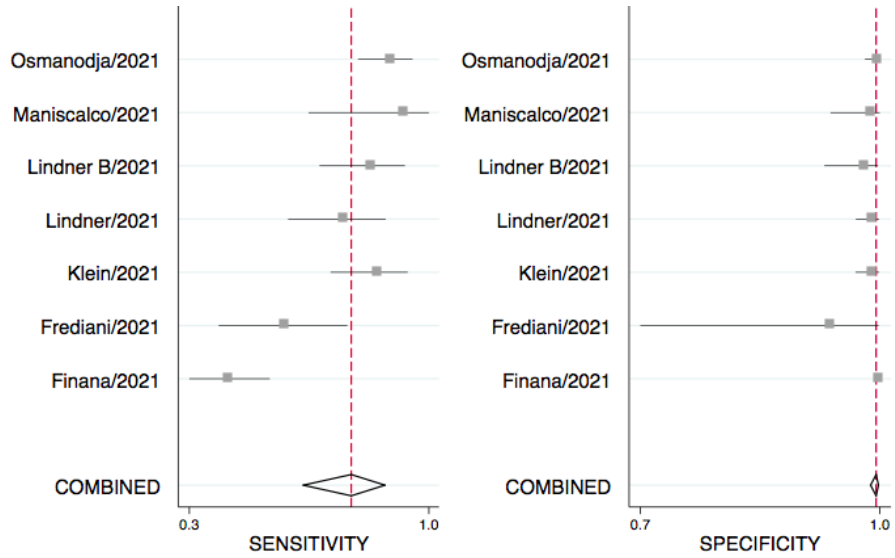


Figure 1. Forest plots of pooled sensitivity and specificity of self-administered RAgTs

B. Subgroup Analysis

Table 1 shows the sensitivity of self-administered RAgTs per subgroup.

Table 1. Subgroup Analysis for Sensitivity of Self-administered RAgTs

Variable	References	No. of Studies (no. of participants)	Sensitivity	95% CI
Presence of symptoms				
Mixed	[10]	1 (105)	0.92	(0.64, 1.00)
Symptomatic	[4-7,9]	5 (883)	0.81	(0.69, 0.89)
Asymptomatic	[4,7,8]	3 (5,765)	0.41	(0.31, 0.53)
Timing of testing in relation to symptoms				
Mixed	[4,5]	2 (577)	0.80	(0.70, 0.87)
Early	[5,7,9]	3 (569)	0.79	(0.62, 0.90)
Asymptomatic	[8]	1 (5,504)	0.40	(0.28, 0.52)
Test brand				
Inflammacheck® device (Exhalation technology LTD, Cambridge, UK)	[10]	1 (105)	0.92	(0.64, 1.00)

Variable	References	No. of Studies (no. of participants)	Sensitivity	95% CI
Dräger Antigen Test SARS-CoV-2 (Dräger Safety AG and Co. KGaA, Lübeck, Germany)	[7]	1 (379)	0.89	(0.79, 0.95)
Panbio™ Ag-RDT (Abbott)	[4]	1 (290)	0.84	(0.71, 0.94)
STANDARD Q COVID-19 Ag Test (SD Biosensor, Korea)	[5.6]	2 (433)	0.79	(0.68, 0.86)
BinaxNOW SARS-CoV-2 (Abbott)	[9]	1 (44)	0.57	(0.37, 0.76)
Innova LFT (Innova Medical Group Inc)	[8]	1 (5,504)	0.40	(0.28, 0.52)
Specimen type				
Exhaled breath condensate	[10]	1 (105)	0.92	(0.64, 1.00)
Nasal mid-turbinate	[4-6]	3 (723)	0.81	(0.73, 0.87)
Anterior nares	[7,9]	2 (423)	0.77	(0.49, 0.92)
Nasal + oropharyngeal	[8]	1 (5,504)	0.40	(0.28, 0.52)
Cycle threshold (Ct) value				
Low (<25)[a]	[4,8]	2 (63)	0.87	(0.86, 0.87)
Mixed[b]	[5-7,9,10]	5 (961)	0.80	(0.68, 0.88)
High (>25)[c]	[4,8]	2 (52)	0.30	(0.05, 0.79)
Methodological quality				
Studies with no serious risk of bias	[5,6]	2 (433)	0.79	(0.68, 0.86)
Studies with serious risk of bias				
related to patient selection	[4,7,10]	3 (774)	0.88	(0.80, 0.93)
related to index test administration	[7-9]	3 (5,927)	0.63	(0.55, 0.70)
related to reference standard administration	[4,9]	2 (334)	0.74	(0.62, 0.84)

[a] One study [8] used Ct values of 18.3-24.4, while another study [4] used 12.7-23.1.
[b] One study [6] used Ct values of 17.3-35.5, while four studies [5,7,9,10] did not report any Ct value.
[c] One study [8] used Ct values of 24.4-35.5, while another study [4] used 23.1-34.5.

By presence of symptoms

The pooled sensitivity of self-administered RAgTs was higher in symptomatic (Sn 0.81, 95% CI 0.69-0.89; n=883; 5 studies) than in asymptomatic individuals (Sn 0.41, 95% CI 0.31-0.53; n=3; 3 studies).

By time of testing in relation to symptom onset

When used during the early phase of the disease (0 to 7 days), the pooled sensitivity of self-administered RAgTs was 0.79 (95% CI 0.62-0.90; n=569; 3 studies). Studies that used self-administered RAgTs in both the early (0 to 7 days) and late phase (>7 days) of the disease had

a pooled sensitivity of 0.80 (95% CI 0.70-0.87; n=577; 2 studies). None of the studies used self-administered RAgTs exclusively during the late phase.

By test brand

Among the brands of RAgTs, ***Inflammacheck® device*** had the highest pooled sensitivity (Sn 0.92, 95% CI 0.64-1.0; n=105). This specific RAgT uses exhaled breath condensate as a test specimen. Two other brands showed a sensitivity of more than 0.80, which include ***Dräger Antigen Test SARS-CoV-2*** (Sn 0.89, 95% CI 0.79-0.95; n=379) and ***Abbott Panbio*** (Sn 0.84, 95% CI 0.71-0.94, n=290). Two studies that used ***STANDARD Q COVID-19 Ag Test*** had a pooled sensitivity of 0.79 (95% CI 0.68-0.86; n=433). Poor sensitivities were demonstrated by two RAgT brands, namely ***Innova LFT*** (Sn 0.40, 95% CI 0.28-0.52; n=5504) and ***BinaxNOW SARS-CoV-2*** (Sn 0.57, 95% CI 0.37-0.76; n=44).

By type of specimen used for the index test

The specimen types with the highest pooled sensitivities were those taken from exhaled breath (Sn 0.92, 95% CI 0.64-1.0; n=105), followed by those taken from the nasal mid-turbinate (Sn 0.81, 95% CI 0.73-0.87; n=723). Anterior nares specimen showed a pooled sensitivity of 0.77 (95% CI 0.49-0.92; n=423). The specimen type with the lowest sensitivity was the combined nasal and oropharyngeal specimens (Sn 0.40, 95% CI 0.28-0.52; n=5,504***.*** This is probably due to the difficulty of taking specimens from the combined nasal and oropharyngeal compared to a nasal swab alone.

By cycle threshold (Ct) value used for the RT-PCR

RAgTs performed better when tested against RT-PCR assays that used lower Ct values of <25 (Sn 0.87, 95% CI 0.86-0.87) compared to those that used higher Ct values of >25 (Sn 0.30, 95% CI 0.05-0.79) as the criterion for classifying positive COVID-19 cases. This may indicate that RAgT is most sensitive when applied to samples with high viral loads.

C. Sensitivity analysis

Self-administered tests showed slightly higher sensitivity when only studies with high methodological quality were included in the analysis (Sn 0.79, 95% CI 0.68-0.86; n=433; 2 studies). Studies with potential risk of bias issues related to the conduct of the RAgT or reference standard reduced the test sensitivity of RAgTs. Studies with potential selection bias tended to inflate the sensitivity estimate (Sn 0.88, 95% CI 0.80-0.93; n=774).

Ongoing Studies on Self-Administered Rapid Antigen Tests

As of October 2021, there were four ongoing studies on self-administered RAgTs evaluating different brands (Biozek, SG Diagnostics, Lucira, and Theram) registered in clinicaltrials.gov.[11-14] All studies evaluate these RAgTs against RT-PCR using conventional sampling methods (trained personnel). Appendix 5 shows the details of the registered studies.

Other Considerations

In the United States of America, a study done by Paltiel et al. showed the clinical and economic effects of widespread home-based antigen testing. A simple compartmental epidemic modelling was used. Compared to no testing at all, the use of home-based antigen testing yielded the following incremental cost-effectiveness ratio: $7,890 per infection averted and $1.43 million per death averted.[15] There is no local data on the economic evaluation of self-administered RAgT.

Results of flex or robustness studies are one of the considerations of WHO for the Emergency Use Listings (WHO EUL) of in vitro diagnostics (IVDs) for detecting SARS-Cov-2.[16] The US

Food and Drug Administration (US FDA) also takes into account flex studies prior to giving Emergency Use Authorization for molecular and antigen diagnostic COVID-10 tests for home use.[17] Flex studies are expected to challenge the kit or system under various conditions of stress. This is to identify potential device deficiencies and determine the robustness (i.e., ability of the test to be unaffected by slight variations) of the kit.[16] The test should still function properly on various conditions of improper use.[18] Examples of conditions that flex studies of RAgTs should consider are the following: multiple skill levels of users (includes reader and reagent problems), specimen and/or reagent volume, operating temperature, visual reading, specimen type, device orientation, and disturbances during analysis.[16,17]

Among the test kits included in this review, Standard Q Covid-19 Ag test (SD Biosensor), Innova LFT (Innova Medical Group), Panbio Ag-RDT (Abbott), and BinaxNow SARS-CoV-2 (Abbott) have approval from foreign agencies.[19-21] However, at the time of the conduct of the included studies in this review, the approval of these brands was for use by trained professionals. Recently, self-test versions of aforementioned RAgT brands were released.[20-23] However, these were not yet the specific kits used in the included studies.

The Philippine Food and Drug Administration (FDA) and the Research Institute of Tropical Medicine (RITM) are currently evaluating the commercially manufactured COVID-19 rapid antigen test kits.[24] However, there is no FDA-approved self-administered rapid antigen test kit. There is no available cost-effective analysis study specific for self-administered RAgT.

In the Philippines, the Department of Health (DOH) issued a memorandum dated September 1, 2021 strictly placing a price cap of Php 960 for RAgTs in all testing and clinical laboratories.[25] Table 2 lists the unit cost of the self-administered RAgT kits used by the studies included in this review.

Table 2. Unit Price of Self-Administered RAgT Kits

Brand	Unit Price per Test
Dräger Antigen Test SARS-CoV-2	Not available
Panbio™ Ag-RDT[a]	Php 520 or USD 13
STANDARD Q COVID-19 Ag Test	Php 550
BinaxNOW SARS-CoV-2 (Abbott)	Php 250 or USD 5
Innova LFT (Innova Medical Group Inc)	Not available
Inflammacheck® device	Not available

[a] 1,000-4975 tests (40-199 boxes)

Recommendations from Other Groups

Table 3 summarizes the recommendations from different agencies, countries, and organizations regarding the use of self-administered RAgTs.

Table 3. Summary of Recommendations from Other Groups

Agency	Recommendation	Date
DOH HTAC [18]	No specific clause on self-administered testing was indicated. However, guidance was provided on providing a minimum of 4-hour long training of healthcare professionals in performing antigen testing to optimize performance.	April 29, 2021
WHO [19]	At present, there is insufficient evidence to make recommendations. Research into potential benefits and harm are still under review.	June 25, 2021
UK NHS [20]	Regular rapid lateral flow tests (twice a week, every 3 to 4 days) are recommended, using the NHS Test and Trace COVID-19 Self-Test kit that can be done by individuals without symptoms of COVID-19.	October 14, 2021
Government of the Netherlands [21]	Rapid antigen self-testing can be done for individuals with no symptoms of COVID-19, specifically for the following situations: 1. Recent travel to the Netherlands from a country with a 'yellow' or 'green' travel advisory 2. Returning to work 3. Returning to school either as a pupil or a staff member 4. Attending classes in secondary vocational education or higher education 5. Childcare worker or a childminder	August 17, 2021
NSW, Australia [22]	Rapid antigen tests are required to be used under the supervision of a health practitioner who has been trained in the correct use of the device and interpretation of results. Trained staff needs to be available onsite to perform or supervise collection of the sample (if self-collected) and to perform the test during the consultation with the health practitioner.	August 2021
Canada [23]	Specimen collection for antigen point-of-care testing may be done with the supervision of a trained individual or done by the person being tested ('self-swabbing'). Self-swabbing with point-of-care antigen test is not currently approved by Health Canada.	August 25, 2021
US CDC [24]	Self-tests may be performed by a person at home or anywhere, provided that all instructions for performing the test must be followed. Self-tests can be used by anyone who is symptomatic regardless of their vaccination status. Unvaccinated persons with no COVID-19 symptoms can also use self-tests, especially if they were potentially exposed to someone with COVID-19.	October 4, 2021

References

[1] World Health Organization. Interim Guidance: Antigen Detection in the Diagnosis of SARS-CoV-2 Infection. Updated 6 October 2021. Accessed at https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays on 26 October 2021.

[2] Burog, AI, Bayona, HH, Cabaluna, IT, Maglente RR. Should rapid antigen tests be used in the diagnosis of COVID-19 in clinically-suspected patients? Evidence Summary. 15 March 2021. PSMID website. Accessed at https://www.psmid.org/rapid-antigen-test-evidence-summary/ on 26 October 2021.

[3] Moisset, X, Gautier, N, Godet, T, et al. Nasopharyngeal swab-induced pain for SARS-CoV-2 screening: A randomised controlled trial of conventional and self-swabbing. *Eur J Pain*. 2021; 25: 924– 929. https://doi.org/10.1002/ejp.1722

[4] Klein JAF, Krüger LJ, Tobian F, Gaeddert M, Lainati F, Schnitzler P, et al. Head-to-head performance comparison of self-collected nasal versus professional-collected nasopharyngeal swab for a WHO-listed SARS-CoV-2 antigen-detecting rapid diagnostic test. Med Microbiol Immunol [Internet]. 2021;210(4):181–6. Available from: https://doi.org/10.1007/s00430-021-00710-9 doi: 10.1007/s00430-021-00710-9

[5] Lindner AK, Nikolai O, Rohardt C, Burock S, Hülso C, Bölke A, Gertler M, Krüger LJ, Gaeddert M, Tobian F, Lainati F, Seybold J, Jones TC, Hofmann J, Sacks JA, Mockenhaupt FP, Denkinger CM. Head-to-head comparison of SARS-CoV-2 antigen-detecting rapid test with professional-collected nasal versus nasopharyngeal swab. Eur Respir J. 2021 May 6;57(5):2004430. doi: 10.1183/13993003.04430-2020.

[6] Lindner AK, Nikolai O, Rohardt C, Kausch F, Wintel M, Gertler M, Burock S, Hörig M, Bernhard J, Tobian F, Gaeddert M, Lainati F, Corman VM, Jones TC, Sacks JA, Seybold J, Denkinger CM, Mockenhaupt FP. Diagnostic accuracy and feasibility of patient self-testing with a SARS-CoV-2 antigen-detecting rapid test. J Clin Virol. 2021 Aug;141:104874. doi: 10.1016/j.jcv.2021.104874.

[7] Osmanodja B, Budde K, Zickler D, Naik M, Hofmann J, Gertler M et al. Accuracy of a Novel SARS-CoV-2 Antigen-Detecting Rapid Diagnostic Test from Standardized Self-Collected Anterior Nasal Swabs. Journal of Clinical Medicine. 2021;10(10):2099.

[8] Garciá-Fiñana M, Hughes DM, Cheyne CP, Burnside G, Stockbridge M, Fowler TA, et al. Performance of the Innova SARS-CoV-2 antigen rapid lateral flow test in the Liverpool asymptomatic testing pilot: Population based cohort study. BMJ. 2021;374:n1367. doi: 10.1136/bmj.n1637

[9] Frediani JK, Levy JM, Rao A, et al. Multidisciplinary assessment of the Abbott BinaxNOW SARS-CoV-2 point-of-care antigen test in the context of emerging viral variants and self-administration. Sci Rep. 2021;11(1):14604. Published 2021 Jul 16. doi:10.1038/s41598-021-94055-1

[10] Maniscalco M, Ambrosino P, Ciullo A, Fuschillo S, Valente V, Gaudiosi C et al. A Rapid Antigen Detection Test to Diagnose SARS-CoV-2 Infection Using Exhaled Breath Condensate by A Modified Inflammacheck® Device. Sensors. 2021;21(17):5710.

[11] Open Label, Single-Center Study Utilizing BIOZEK COVID-19 Antigen Rapid Test [Internet]. 2021 [cited 26 Oct 21] Available from: https://clinicaltrials.gov/ct2/show/NCT04926779?term=NCT04926779&draw=2&rank=1

[12] COVID-19 Antigen Rapid Test Kit (SETCOV) [Internet]. 2021 [cited 26 Oct 21] Available from: https://clinicaltrials.gov/ct2/show/NCT04889365?term=NCT04889365&draw=2&rank=1

[13] A Study to Evaluate the Performance of the Lucira Health All-in-One COVID-19 Test Kit vs Hologic Panther Fusion [Internet]. 2021 [cited 26 Oct 21] Available from: https://clinicaltrials.gov/ct2/show/NCT04720794?term=NCT04720794&draw=2&rank=1

[14] Study to Evaluate the Performance of the Therma COVID-19 Rapid Antigen Test for Detection of SARS-CoV-2 [Internet]. 2021 [cited 26 Oct 21] Available from: https://clinicaltrials.gov/ct2/show/NCT04878068?term=NCT04878068&draw=2&rank=1

[15] Paltiel AD, Zheng A, Sax PE. Clinical and economic effects of widespread rapid testing to decrease SARS-CoV-2 transmission. Ann Intern Med. 2021;174(6):803–10. doi: https://doi.org/10.7326/M21-0510

[16] World Health Organization. Instructions and requirements for Emergency Use Listing (EUL) submission: In vitro diagnostics detecting SARS-CoV-2 nucleic acid and rapid diagnostics tests detecting SARS-CoV-2 antigens. Version 5. 2021 Jun.

[17] Food and Drug Administration. Template for Developers of Molecular and Antigen Diagnostic COVID-19 Tests for Home Use. 2021 Nov.

[18] Medical Device Innovation Consortium. Developing Clinical Evidence for Regulatory and Coverage Assessments in In Vitro Diagnostics (IVDs). 2019 Aug.

[19] World Health Organization. WHO Emergency Use Listing for In vitro diagnostics (IVDs) Detecting SARS-CoV-2. 2021 Apr.

[20] Center for Devices, Radiological Health. In Vitro Diagnostics EUAs - Antigen Diagnostic Tests for SARS-CoV-2 [Internet]. Fda.gov. 2021 [cited 2021 Nov 13]. Available from: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-antigen-diagnostic-tests-sars-cov-2

[21] Innova rapid antigen test [Internet]. 2021 [cited 2021 Nov 13]. Available from: https://innovamedgroup.com/innova-rapid-antigen-test/

[22] SD BIOSENSOR [Internet]. Sdbiosensor.com. [cited 2021 Nov 13]. Available from: https://www.sdbiosensor.com/product/product_view?product_no=295

[23] PanbioTM COVID-19 Antigen Self-Test [Internet]. Globalpointofcare.abbott. [cited 2021 Nov 13]. Available from: https://www.globalpointofcare.abbott/en/product-details/panbio-covid-19-antigen-self-test.html

[24] EVALUATION OF RAPID Ag TEST KITS [Internet]. Gov.ph. [cited 2021 Nov 6]. Available from: https://ritm.gov.ph/covid-19-kit-evaluation/completed-evaluations/sars-cov-2-rapid-antigen-ag-test

[25] Department of Health. Price Cap for COVID-19 Rapid Antigen Testing – Asian Preparedness Partnership (APP) [Internet]. App.adpc.net. 26 October 2021. Accessed from: https://app.adpc.net/resources/price-cap-for-covid-19-rapid-antigen-testing/

[26] Department of Health Health Technology Assessment Council. Evidence Summary for Rapid Antigen Test - Recommendations. 29 April 2021. Accessed https://hta.doh.gov.ph/wp-content/uploads/2021/05/2021_Evidence_Summary_for_Rapid_Antigen_Test-Recommendation.pdf on 26 October 2021.

[27] World Health Organization. Recommendations for national SARS-CoV-2 testing strategies and diagnostic capacities. 15 June 2021. Accessed https://apps.who.int/iris/bitstream/handle/10665/342002/WHO-2019-nCoV-lab-testing-2021.1-eng.pdf?sequence=1&isAllowed=y on 26 October 2021.

[28] GOV.UK. Guidance for patients, the public and professional users: a guide to COVID-19 tests and testing kits [Internet]. 5 October 2021. Accessed https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/for-patients-the-public-and-professional-users-a-guide-to-covid-19-tests-and-testing-kits on 26 October 2021.

[29] Government of Netherlands. Coronavirus self-tests [Internet]. 17 August 2021. Accessed https://www.government.nl/topics/coronavirus-covid-19/coronavirus-test/coronavirus-self-tests/when-to-use-a-covid-self-test on 26 October 2021.

[30] Nsw.gov.au. [Internet]. Rapid antigen testing. 8 October 2021. Accessed https://www.nsw.gov.au/covid-19/stay-safe/testing/how-testing-works/rapid-antigen-testing on 26 October 2021.

[31] Health.gov.on.ca. [Internet]. COVID-19 Guidance: Considerations for Antigen Point-of-Care Testing 26 October 2021. Accessed from: https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/Antigen_Screening_Guidance_2021-03-5.pdf on 26 October 2021.

[32] COVID-19 and Your Health [Internet]. Centers for Disease Control and Prevention. 2021. 26 October 2021. Accessed from: https://www.cdc.gov/coronavirus/2019-ncov/testing/self-testing.html on 26 October 2021.

Appendix 1. Evidence to Decision

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Problem	No	Yes (9)					
Certainty of Evidence	High	Moderate (4)	Low (5)	Very low			Overall, the studies included are of moderate methodological quality. Two studies are of high quality. Five studies are of moderate quality due to unclear issues on patient selection, index test and reference standard.
Accuracy	Very Accurate	Accurate (8)	Inaccurate (1)	Very Inaccurate			Across 7 studies, the pooled sensitivity of self-administered RAgTs was found to be moderate at 0.77 (95%CI: 0.62-0.87), with high heterogeneity (I^2 = 94%). Pooled specificity was excellent at 0.996 (95%CI: 0.99-1.00).
Values	Important uncertainty or variability (2)	Possibly important uncertainty or variability (6)	Possibly NO important uncertainty or variability (1)	No important uncertainty or variability			
Resources Required	Uncertain	Large cost	Moderate Cost (6)	Negligible cost	Moderate savings	Large savings (3)	The cost per unit of each rapid antigen test ranges from Php 250 to Php 500.
Certainty of evidence of required resources	No included studies (2)	Very low	Low (5)	Moderate (2)	High		In the Philippines, the Department of Health issued a memorandum dated September 1, 2021 strictly placing a price cap of Php 960 for rapid antigen testing in all testing and clinical laboratories.
Cost effectiveness	No included studies (5)	Favors RT-PCR (2)	Does not favor either RAgT or RT-PCR	Favors RAgT (2)			No local cost-effectiveness studies are available as of press time on comparing self-administered rapid antigen tests and RT-PCR.
Equity	Uncertain (6)	Reduced	Probably no impact	Increased (3)			
Acceptability	Uncertain (4)	No (2)	Yes (3)				
Feasibility	Uncertain (3)	No	Yes (6)				

Appendix 2. Search Yield and Results

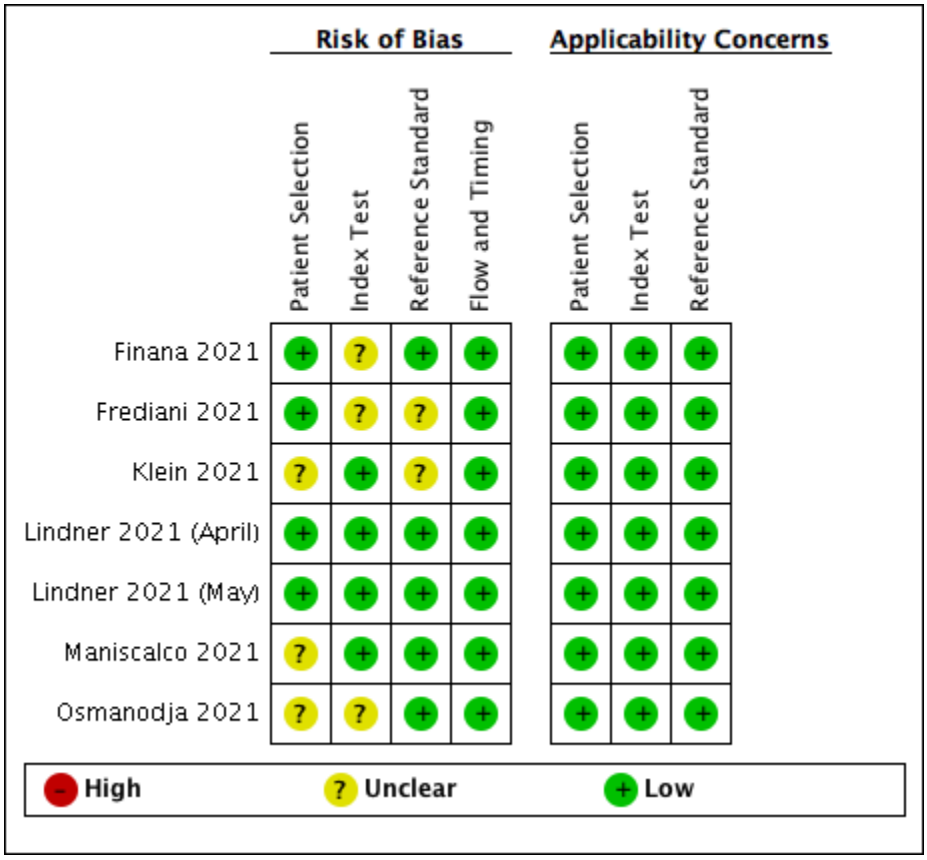
Search	Query	Results	Time
#9	Search **#1 and #8** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	475	02:52:17
#8	Search **#7 OR #2** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	1,017	02:51:40
#7	Search **#5 OR #6** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	1,016	02:51:26
#6	Search: **rapid antigen test* OR "rapid antigen detection test" OR radt OR radts OR rdt OR rdts OR (antigen* n3 detect*)** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	1,016	02:51:17
#5	Search **#3 and #4** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	9	02:51:05
#4	Search: **(test OR tests OR detect* OR diagnos* OR kit OR kits OR assay*)** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	413,770	02:50:56
#3	Search: **((rapid OR point-of-care OR "point of care" OR poc OR poct) n3 antigen))** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	9	02:50:45
#2	Search: **"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"** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	13	02:50:29
#1	Search: **("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)** Filters: **from 2021/3 - 2021/9/14** Sort by: **Most Recent**	77,879	02:50:18

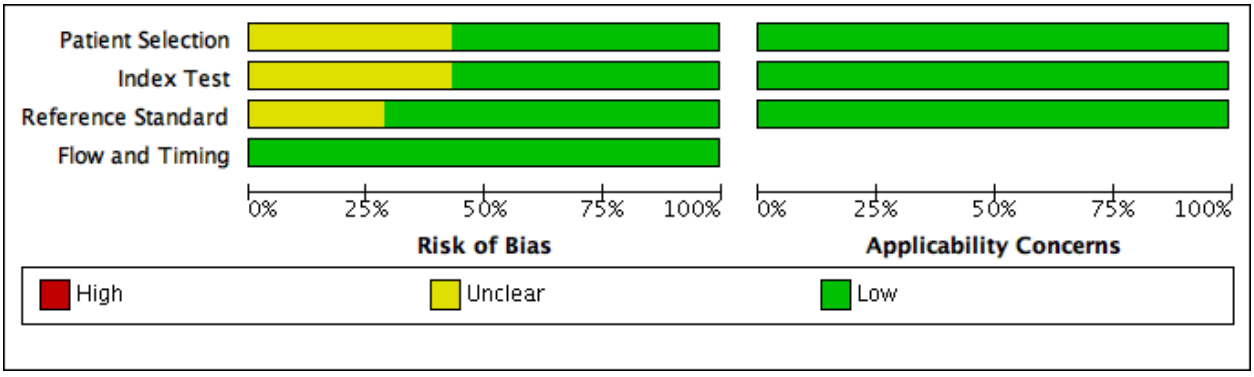
Appendix 3. Characteristics of Included Studies

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference Standard	
						Test	Specimen
Lindner 2021 [5]	Germany	STANDARD Q COVID-19 Ag Test (SD Biosensor, Korea)	NMT for self-administered, NP for staff-collected	Symptomatic patients at ambulatory testing facility (community setting)	146	RT-PCR (not specified)	NP/OP
Lindner 2021 [6]	Germany	STANDARD Q COVID-19 Ag Test (SD Biosensor, Korea)	NMT for self-administered, NP for staff-collected	Symptomatic patients at ambulatory testing facility (community setting)	287	Roche Cobas and Tib Molbiol®	NP/OP
Maniscalco 2021 [10]	Italy	Inflammacheck® device (Exhalation technology LTD, Cambridge, UK)	Exhaled breath condensate	≥ 18 y/o with or without symptoms in a community setting	105	NeumoDx	NP
Osmanodja 2021 [7]	Germany	Dräger Antigen Test SARS-CoV-2 by Dräger Safety AG and Co. KGaA (Lübeck, Germany)	Anterior Nares	≥ 18 y/o with or without symptoms in a community setting	379	Roche Cobas SARS-CoV-2 assay (Pleasanton, CA, USA)	NP and OP
Fiñana 2021 [8]	UK	Innova LFT	Combined throat and nose	> 18 y/o with or without symptoms in a community setting	5504	TaqPath; ThermoFisher Scientific	Combined throat and nose (also collected by participant)
Klein 2021 [4]	Germany	Panbio™ Ag-RDT	NMT for self-administered, NP for staff-collected	Symptomatic adults and high-risk contacts of confirmed SARS-Cov-2 in an in-drive in testing center (community setting)	290	Tib Molbiol®	NP
Frediani 2021 [9]	USA	BinaxNOW SARS-CoV-2 (Abbott)	Anterior nares	> 7 y/o (adults and pedia) symptomatic within 7 days from onset in community-based and hospital-based testing center (community setting)	44 self-collected; 297 staff-collected	Cobas 6800 (Roche Diagnostics), Abbott Alinity (Abbott Labs), Panther Fusion (Hologic)	NP

NMT: Nasal midturbinate; NP: Nasopharyngeal; OP: Oropharyngeal.

Appendix 4. Risk of Bias and Applicability Concerns of Included Studies





Appendix 5. Characteristics of Ongoing Studies

Title / Study Design / NCT	Population	Intervention	Comparator	Outcomes	Status
Open Label, Single-Center Study Utilizing BIOZEK COVID-19 Antigen Rapid Test [11] • Open-label, single-center study • Quality Research and Invention LLC, Southampton, New York, USA • NCT04926779	**Inclusion Criteria** ∉≥18 y/o and have had an RT-PCR test performed prior to enrollment. ∉Able to understand and willingly sign a written informed consent ∉Needs to meet at least 1 of the following: ○ Currently experiencing symptoms of COVID-19 ○ Clinically diagnosed or suspected to have COVID-19 ○ Recent past (3 weeks) exhibited symptoms of COVID-19 ○ Capable of performing a self-collection of a nasopharyngeal sample with use of nasal swab kit ○ Capable of performing a self-collection of an oral fluid sample with use of oral fluid collection kit ○ Interacted with a COVID-19 positive individual **Exclusion Criteria** ∉Cannot perform self-collection of a nasopharyngeal sample with use of nasal swab kit ∉Cannot perform self-collection of an oral fluid sample with use of oral fluid collection kit ∉Have a deviated nasal septum ∉Cognitively impaired individuals resulting in the inability to provide informed consent	Biozek COVID-19 Antigen Rapid Test Results Performed on Self-collected Samples	COVID-19 RT-PCR as a Standard of Care	**Primary** • Sensitivity and Specificity of Biozek Covid-19 Antigen Rapid Test (Saliva) • Sensitivity and Specificity of Biozek Covid-19 Antigen Rapid Test (Nasopharyngeal Swab)	**Recruiting** **Study start**: May 24, 2021 **Primary completion**: September 20, 2021 **Study completion**: September 20, 2021
COVID-19 Antigen Rapid Test Kit (SETCOV) [12] • Prospective cohort study (Observational) • Polish Society of Disaster Medicine • NCT04889365	Volunteers with or without COVID-19 symptoms **Inclusion Criteria** ● Adult (aged ≥ 18 years) volunteers **Exclusion Criteria** ∉Children (aged < 18years)	SG Diagnostics COVID-19 Antigen Rapid Test Kit (self-use)	Polymerase chain reaction (PCR) test	**Primary** ● Sensitivity of SG Diagnostics COVID-19 Antigen Rapid Test Kit ● Specificity of SG Diagnostics COVID-19 Antigen Rapid Test Kit	**Active, not recruiting** **Study start**: May 11, 2021 **Primary completion**: June 30, 2021 **Study completion**: July 10, 2022

Title / Study Design / NCT	Population	Intervention	Comparator	Outcomes	Status
A Study to Evaluate the Performance of the Lucira Health All-in-One COVID-19 Test Kit vs Hologic Panther Fusion [13] • Open label, single group assignment • Lucira Health Inc. • NCT04720794	**Inclusion Criteria** • Ages 18-75 • Must be able to read and write in English or Spanish • Must be willing to try rapid COVID-19 test and self-collect a nasal swab sample in both nostrils • Must be one of the following: ○ Currently experiencing a fever of 100˙ Fahrenheit and above or self-reports having fever within the past 48 hours and experiencing at least one (1) additional associated CDC COVID-19 symptoms. ○ Previously tested positive for COVID-19 in past 14 days, and experiencing at least one (1) additional associated CDC COVID-19 symptom ○ Currently experiencing at least three (3) additional associated CDC COVID-19 symptoms so long as at least at least one (1) symptom is either: cough, shortness of breath, and/or new loss of taste or smell. **Exclusion Criteria** • Currently suffering from nasal trauma such as a nosebleed • Received a nasal rinse/wash/aspirate for standard of care testing	Lucira COVID-19 All-In-One test kit (self-collected)	Hologic Panther Fusion RT-PCR assay	**Primary** • COVID-19 Prevalence Rate/Expected Values counts • COVID-19 Prevalence Rate/Expected Values percentages **Secondary** • Collection Performance/Incidence Rate counts • Collection Performance/Incidence Rate percentages • Sensitivity and specificity **Other measures** • Invalid rates	**Completed** **Study start**: September 25, 2020 **Primary completion**: October 20, 2020 **Study completion**: October 20, 2020
Study to Evaluate the Performance of the Therma COVID-19 Rapid Antigen Test for Detection of SARS-CoV-2 [14] • Retrospective Cohort, observational • Cannabis Research Associates • NCT04878068	Potential participants attending a COVID-19 testing centre for a PCR test will be approached to determine eligibility and obtain consent after they have had their PCR test completed. Three hundred participants will be recruited into the study.	Theram COVID-19 Rapid Antigen Test (self-collected)	COVID-19 RT-PCR Test	**Primary** • Establish Performance of Therma COVID-19 Rapid Antigen Test **Secondary** • Participant Feedback • User Feedback	**Not yet recruiting** **Study start**: May 15, 2021 **Estimated Primary completion**: June 30, 2021 **Estimated Study completion**: June 30, 2021

Appendix 6. GRADE Evidence Profile

Should self-administered rapid antigen test be used to diagnose COVID-19 in symptomatic individuals?

Patient or population: symptomatic individuals
Setting: Community
New test: Self-administered rapid antigen tests
Cut-off value: Not applicable
Pooled sensitivity: 0.81 (95% CI: 0.69 to 0.89)
Pooled specificity: -- (95% CI: -- to --)

Outcomes	No of studies (patient)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test Accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication Bias	Pre-test probability of 5%	Pre-test probability of 10%	Pre-test probability of 20%	
True positives (patients with COVID-19)	5 studies (750 patients)	Cross-sectional (cohort type accuracy study)	serious[a]	not serious	serious[b]	not serious	none	41 (34 to 45)	81 (69 to 89)	162 (138 to 178)	⊕⊕◯◯ Low
False negatives (patients incorrectly classified as not having COVID-19)								9 (5 to 16)	19 (11 to 31)	38 (22 to 62)	
True negatives (patients without COVID-19)	5 studies (750 patients)	Cross-sectional (cohort type accuracy study)	serious[a]	not serious	Not serious	not serious	none	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	⊕⊕◯◯ Low
False positives (patients incorrectly classified as having COVID-19)								950 (950 to 950)	900 (900 to 900)	800 (800 to 800)	

CI: confidence interval

Explanations
a. Unclear issues in patient selection and conduct of index test and reference standard
b. Significant heterogeneity among included studies

Should self-administered rapid antigen test be used to diagnose COVID-19 in asymptomatic individuals?

Patient or population: asymptomatic individuals
Setting: Community
New test: Self-administered rapid antigen tests
Cut-off value: Not applicable
Pooled sensitivity: 0.41 (95% CI: 0.31 to 0.53)
Pooled specificity: -- (95% CI: -- to --)

Outcomes	No of studies (patient)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test Accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication Bias	Pre-test probability of 5%	Pre-test probability of 10%	Pre-test probability of 20%	
True positives (patients with COVID-19)	3 studies (5,765 patients)	Cross-sectional (cohort type accuracy study)	serious[a]	not serious	serious[b]	not serious	none	21 (16 to 27)	41 (31 to 53)	82 (62 to 106)	⊕⊕◯◯ Low[a,b]
False negatives (patients incorrectly classified as not having COVID-19)								29 (23 to 34)	59 (47 to 69)	118 (94 to 138)	
True negatives (patients without COVID-19)	5 studies (5,765 patients)	Cross-sectional (cohort type accuracy study)	serious[a]	not serious	Not serious	not serious	none	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	⊕⊕◯◯ Low[a,b]
False positives (patients incorrectly classified as having COVID-19)								950 (950 to 950)	900 (900 to 900)	800 (800 to 800)	

CI: confidence interval

Explanations

a. Unclear issues in patient selection and conduct of index test and reference standard
b. Significant heterogeneity among included studies