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 DOH AHEAD Program through the PCHRD

EVIDENCE SUMMARY

Should rapid antigen tests be used in the diagnosis of COVID-19 in clinically suspected patients?

Evidence Reviewers: Aldrich Ivan Lois D. Burog, MD, MSc (cand.), Howell Henrian G. Bayona, MSc, MSc (cand.), Ian Theodore G. Cabaluna, MD, RPh, GDip (Epi), Renee Rose O. Maglente, RN, GDip (Clinical Epidemiology)

RECOMMENDATIONS

We recommend the use of rapid antigen test under all these conditions in patients suspected of COVID-19 infection: *(Moderate quality of evidence; Strong recommendation)*

- Symptomatic AND
- Early phase </=7 days from onset of symptoms AND
- Specific brands that demonstrated sensitivity ≥80% and have very high specificity (≥97-100%)

We recommend against the use of saliva as a specimen for rapid antigen test in patients suspected of COVID-19 infection. *(Moderate quality of evidence; Strong recommendation)*

We recommend against the use of rapid antigen test alone in diagnosing COVID-19 in asymptomatic patients suspected of COVID-19 infection. *(Moderate to high quality of evidence; Strong recommendation)*

Consensus Issues

There were only two studies that used saliva as a specimen for rapid antigen test, which produced a pooled sensitivity of 17% (95% CI 13-23%) and a pooled specificity of 99% (95% CI 99-100%). Given the current evidence of the very low sensitivity for saliva, qualifying which specimen is used for a rapid antigen test is necessary.

Key Findings

Moderate quality evidence from 30 studies and 10 evaluation reports showed that the pooled sensitivity of RAgTs is 72% (95%CI: 64 to 78; I2 = 95.77). The specificity of RAgTs remained consistently very high in all studies, with a pooled specificity of 99%. The sensitivity of the RAgTs varied widely across studies, with higher sensitivity estimates noted for specific test brands, symptomatic patients, and nasopharyngeal/nasal swab specimens.

Introduction

Detection of SARS-CoV-2 by nucleic acid amplification test (NAAT), such as reverse-transcription polymerase chain reaction (RT-PCR) remains the “gold standard” in confirming the diagnosis of COVID-19 infection. Recently, immunoassays such as antigen tests that detect presence of a specific viral antigen are now available with a faster turnaround time and the option of more frequent testing compared to the RT-PCR. These antigen tests are relatively inexpensive compared to RT-PCR and may be used at point-of-care. Clinical performance of any rapid antigen diagnostic test is dependent on the context of its use [1].

In a rapid review published by by the DOH HTA Council (September 2020), the pooled sensitivity of RAgT was found to be low at 49% (95%CI: 28 to 70%) but with a high pooled specificity of 99% (95% CI: 98 to 100) across 9 studies. At that time, the HTAC did not recommend use of rapid antigen tests for non-targeted use in mass screening or in the diagnosis of COVID-19 among individuals with low index of suspicion (i.e., no symptoms and no history of exposure) [2].

This review aimed to update the existing pooled evidence synthesized at that time and to determine diagnostic accuracy of rapid antigen tests compared to RT-PCR in the diagnosis of COVID-19.

Review Methods

We conducted a literature search for studies published in 2019 to February 7, 2021 on MEDLINE using medical subject headings combined with free 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.

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 20 January 2021. 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). Local publications such as health technology assessments on the use of rapid antigen tests were also sought out.

Results

Overall, 331 of records were identified from primary databases and additional sources. A total of 30 studies [3-32] and 10 evaluation reports [33-42] met the pre-specified eligibility criteria. There were 17 different rapid antigen test brands evaluated across the different studies and evaluation reports with a (n = 41,230 patient and samples) that compared rapid antigen testing using different anterior nasal, nasopharyngeal, oropharyngeal or saliva specimens to RT-PCR using mostly nasopharyngeal specimens. See Appendix 1 for the Characteristics of Included Studies.

Overall, the methodological quality of included studies was rated moderate. There were 4 studies with high quality [4,8-9, 32], 16 studies [3,5,11-13, 15-17, 19-20, 23-24, 26, 28-29, 31] and 10 evaluation reports [33-42] with moderate quality and 10 studies with low quality [6,7,10,14,18,21,22,25,27,30].

Overall diagnostic accuracy

Overall, the pooled sensitivity of RAgTs was 72% (95%CI: 64 to 78; I^2 = 95.77) (**Figure 1**). The sensitivity of the RAgTs varied widely across different test brands and study populations, ranging from 0 to 100%. In contrast, the specificity of RAgTs remained consistently very high in all studies, with a pooled specificity of 99% (95% CI: 99 to 100; I^2 = 93.16).

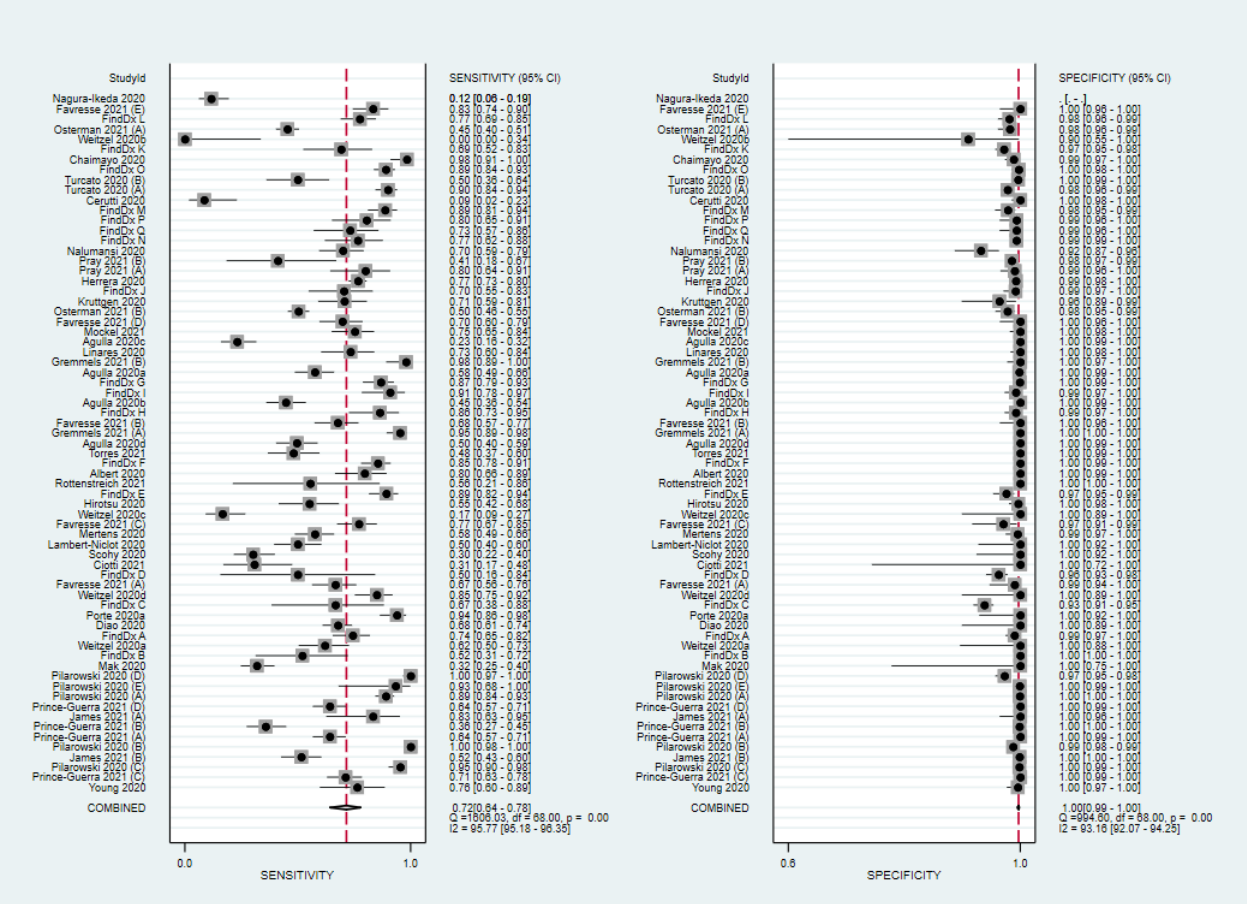

Figure 1. Pooled paired forest plots showing individual and pooled sensitivity and specificity estimates of rapid antigen tests for SARS-CoV-2.

Subgroup analysis

In this review, substantial heterogeneity was expected for the pooled estimates of diagnostic tests. Hence, pre-specified subgroup analysis was planned a priori to determine the factors that may affect the pooled sensitivity and specificity of rapid antigen tests. Specifically, subgroup analysis was done according to test brand, presence of symptoms, timing of testing and type of specimen used. Results of these subgroup analyses are summarized in Tables 1 to 4.

A. Effect of test brand

Sensitivity estimates varied across the different brands of rapid antigen tests and within the studies (Table 1). Based on 11 studies (n = 16060) with moderate to high methodological quality, the ***BinaxNOQ COVID-19 Card*** (Abbott Diagnostics) test kit showed the highest pooled sensitivity at 90% (95% CI: 0.66 to 0.93). Other test brands that had 80% sensitivity or higher were the following: ***NowCheck COVID-19 Ag Test*** (Bionote Inc) at 89% (95% CI: 81 to 95), ***VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Test*** at 80% (95% CI: 74 to 90), and ***Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit*** at 80% (95% CI: 62 to 91; I^2=0%)

Table 1. Diagnostic accuracy of rapid antigen tests according to brand (n = 17 brands)

	No. of studies (samples)	Sensitivity	95% CI	Specificity	95% CI	I^2
BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	11 (16060)	0.90	0.66-0.93	1.00	1.00-1.00	99
NowCheck COVID-19 Ag Test Bionote Inc	2 (1726)	0.89	0.81-0.95	1.00	1.00-1.00	-

	No. of studies (samples)	Sensitivity	95% CI	Specificity	95% CI	I^2
VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test	1 (188)	0.80	0.74-0.90	0.92	0.96-1.00	NA
Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit	4 (1204)	0.80	0.62-0.91	1.00	0.26-1.00	0
Biotical SARS-CoV-2 Ag	1 (188)	0.67	0.56-0.76	0.99	0.94-1.00	-
STANDARD Q COVID19 Ag (SD-Biosensor)	10 (6932)	0.77	0.58-0.94	0.99	0.98-1.00	98
Healgen Coronavirus Ag Rapid Test	1 (188)	0.77	0.67-0.85	0.97	0.91-0.99	-
Panbio COVID-19 Ag Rapid Test	14 (5222)	0.76	0.61-0.86	1.00	1.00-1.00	88
BD Veritor System (Veritor)	1 (251)	0.76	0.60-0.89	1.00	0.97-1.00	-
Sofia SARS Antigen Fluorescent Immunoassay testing	3 (2270)	0.70	0.53-0.85	0.99	0.98-0.99	78
Roche SARS-CoV-2 Rapid Antigen Test	4 (1380)	0.66	0.55-0.75	0.99	0.97-1.00	0
STANDARD™ F COVID-19 Ag FIA (FIA) SD Biosensor	3 (1810)	0.64	0.40-0.85	0.97	0.96-0.98	96
BIOCREDIT COVID-19 Ag test	4 (1997)	0.55	0.38-0.71	1.00	0.91-1.00	86
LUMIPULSE SARS-CoV-2 Ag	1 (313)	0.55	0.42-0.68	1.00	0.98-1.00	-
Coris Coronavirus Disease 2019 Ag Respi-Strip test	5 (1081)	0.44	0.31-0.58	0.99	0.84-1.00	0
Huaketai New Coronavirus (SARS-CoV-2) N Protein Detection Kit FIA	1 (109)	0.17	0.09-0.27	1.00	0.89-1.00	-
StrongStep COVID-19 Antigen Test	1 (19)	0.00	0.00-0.34	0.90	0.55-1.00	-

B. Effect of presence of symptoms

The pooled sensitivity of rapid antigen tests was higher when used among symptomatic patients (n=12,559) at 78% (95% CI: 69 to 86; I^2=99%; 26 studies). Among asymptomatic patients (n = 10,937), sensitivity was lower at 51% (95% CI: 39 to 63; I^2=0.49, 7 studies). See Table 2.

Table 2. Summary of studies on rapid antigen tests stratified according to presence of symptoms among patients tested for COVID-19

	No. of studies (samples)	Sensitivity	95% CI	Specificity	95% CI	I^2	LR+	LR-
Symptomatic	30 (12559)	0.78	0.69-0.86	1.00	0.99-1.00	99%	298.8	0.22
Mixed	32 (8964)	0.67	0.56-0.77	1.00	0.99-1.00	99%	142.9	0.33
Non-symptomatic	7 (10937)	0.51	0.39-0.63	1.00	0.99-1.00	78%	310.4	0.49

C. Effect of timing of testing in relation to onset of symptoms

Based on 12 studies, the pooled sensitivity estimate was 71% (95% CI: 44 to 89) when used for testing patients in the early phase of the disease (0 to 7 days; n = 3683). This was higher compared to the resulting sensitivity estimate of .65% (95% CI: 57 to 71) for those tested in the late phase (8 to 14 days; n =831) (Table 3). This finding needs further validation studies as the number of participants and studies including late phase was small.

Table 3. Pooled sensitivity and specificity of rapid antigen tests stratified by phase of the disease

	No. of studies	Sensitivity	95% CI	Specificity	95% CI	I^2	LR+	LR-
Early and late	16	0.81	0.76 to 0.85	0.99	0.98-1.00	95%	283.6	0.32
Early	12	0.71	0.44 to 0.89	1.00	0.99-1.00	97%	308.1	0.29
Unknown	40	0.68	0.57 to 0.77	1.00	0.99-1.00	99%	98.48	0.34
Late	2	0.65	0.57 to 0.71	0.99	0.99-1.00	-	65	0.35

D. Effect of type of specimen used

Rapid antigen tests that used anterior nares swab specimens alone had the highest pooled sensitivity of 84% (95%CI: 66 to 93) based on 15 studies (n = 2,004) followed by nasopharyngeal swab specimen alone with a sensitivity of 72% (95% CI: 65 to 78) across 36 studies (n = 1080). On the other hand, rapid antigen tests using saliva as the specimen had the lowest pooled sensitivity at 17% (95% CI: 13 to 23) across 2 studies (n = 762).

Table 4. Pooled sensitivity and specificity of rapid antigen tests stratified by type of specimen used.

Type of specimen	No. of studies (samples)	Sensitivity	95% CI	Specificity	95% CI	I^2	LR+	LR-
Anterior nares	15 (2004)	0.84	0.66-0.93	1.00	0.99-1.00	99%	380.3	0.17
Nasopharyngeal alone	36 (1080)	0.72	0.65-0.78	1.00	0.99-1.00	99%	230.7	0.28
Naso- and oropharyngeal	16 (65)	0.65	0.47-0.79	0.99	0.97-1.00	96%	59.5	0.36
Saliva	2(762)	0.17	0.13-0.23	0.99	0.99-1.00	99%	54.18	0.78

Recommendations from Other Groups

Table 5 summarizes recommendations from different agencies and organizations regarding the use of rapid antigen tests for the diagnosis of COVID-19.

Table 5. Recommendation summary from other guidelines and agencies regarding the use of rapid antigen tests for the diagnosis of COVID-19, level of evidence, strength of recommendation and the date of latest update.

Agency	Recommendation	Date
IDSA	IDSA guidelines made no recommendations for or against using rapid tests (i.e., result time ≤ 1 hour) versus standard RNA testing in symptomatic individuals suspected of having COVID-19, citing knowledge gaps.	3 Dec 2020
NIH	No current recommendations available regarding the use of rapid antigen test	11 Feb 2021
CDC	Evaluation of antigen testing results should take into consideration the: • context of its use (i.e., clinical diagnosis, screening) • performance characteristics (i.e., sensitivity, specificity) • prevalence of SARS-CoV-2 infection in the community, • and the clinical context surrounding the patient to be tested. CDC has stated it may be needed to confirm results of the antigen test with another test (i.e., NAAT). CDC testing algorithm recommends additional NAAT testing when a person who is strongly suspected of having SARS-CoV-2 infection (i.e., symptomatic) receives a negative result, and when a person who is asymptomatic receives a positive result.	16 Dec 2020
WHO	SARS-CoV-2 Ag-RDTs that meet the minimum performance requirements of ≥80% sensitivity and ≥97% specificity compared to a NAAT reference assay1 can be used to diagnose SARS-CoV-2 infection in a range of settings where NAAT is unavailable or where prolonged turnaround times preclude clinical utility.	11 Sep 2020
DOH HTAC	HTAC does not recommend the use of rapid antigen tests for indiscriminate use in mass screening (e.g., returning overseas Filipino workers (OFWs), return-to-work clearance, tourist clearance, land-stranded individuals (LSIs)) and COVID-19 diagnosis in individuals with low index of suspicion (i.e., asymptomatic and no history of exposure).	2 Oct 2020
DOH DM 2020-0468	The use of antigen tests is not recommended in settings with an expected low prevalence of disease or populations with no known exposure, such as among asymptomatic travelers or for border control.	26 Oct 2020

Research Gaps

As of February 8, 2021, there are 20 ongoing clinical trials on antigen tests for the diagnosis of COVID-19 registered in ClinicalTrial.gov and finddx.org. The earliest results are expected to be completed on June 30, 2021. See Appendix 3 and 4.

References

[1] Labs [Internet]. Centers for Disease Control and Prevention. 2021 [cited 19 February 2021]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html

[2] Use of Rapid Antigen Test Kits for the Diagnosis of COVID-19 | HTA [Internet]. Hta.doh.gov.ph. 2021 [cited 19 February 2021]. Available from: https://hta.doh.gov.ph/2020/10/15/use-of-rapid-antigen-test-kits-for-the-diagnosis-of-covid-19/

[3] Agulló V, Fernández-González M, Ortiz de la Tabla V, Gonzalo-Jiménez N, García JA, Masiá M et al. Evaluation of the rapid antigen test Panbio COVID-19 in saliva and nasal swabs in a population-based point-of-care study. Journal of Infection. 2020 Jan 1. https://doi.org/10.1016/j.jinf.2020.12.007

[4] Albert E, Torres I, Bueno F, Huntley D, Molla E, Fernández-Fuentes M et al. Field evaluation of a rapid antigen test (Panbio™ COVID-19 Ag Rapid Test Device) for COVID-19 diagnosis in primary healthcare centres. Clinical Microbiology and Infection. 2020;.

[5] Cerutti F, Burdino E, Milia M, Allice T, Gregori G, Bruzzone B et al. Urgent need of rapid tests for SARS CoV-2 antigen detection: Evaluation of the SD-Biosensor antigen test for SARS-CoV-2. Journal of Clinical Virology. 2020;132:104654.

[6] Chaimayo, C., Kaewnaphan, B., Tanlieng, N. *et al.* Rapid SARS-CoV-2 antigen detection assay in comparison with real-time RT-PCR assay for laboratory diagnosis of COVID-19 in Thailand. *Virol J* **17,** 177 (2020). https://doi.org/10.1186/s12985-020-01452-5

[7] Ciotti M, Maurici M, Pieri M, Andreoni M, Bernardini S. Performance of a rapid antigen test in the diagnosis of SARS-CoV-2 infection. Journal of Medical Virology. 2021;.

[8] Diao B, Wen K, Zhang J, Chen J, Han C, Chen Y et al. Accuracy of a nucleocapsid protein antigen rapid test in the diagnosis of SARS-CoV-2 infection. Clinical Microbiology and Infection. 2021;27(2):289.e1-289.e4.

[9] Favresse J, Gillot C, Oliveira M, Cadrobbi J, Elsen M, Eucher C et al. Head-to-Head Comparison of Rapid and Automated Antigen Detection Tests for the Diagnosis of SARS-CoV-2 Infection. Journal of Clinical Medicine. 2021;10(2):265.

[10] Gremmels H, Winkel B, Schuurman R, Rosingh A, Rigter N, Rodriguez O et al. Real-life validation of the Panbio™ COVID-19 antigen rapid test (Abbott) in community-dwelling subjects with symptoms of potential SARS-CoV-2 infection. EClinicalMedicine. 2021;31:100677.

[11] Herrera V, Hsu V, Adewale A, Johnson L, Hendrix T, Kuhlman J et al. Testing Healthcare Workers Exposed to COVID19 using Rapid Antigen Detection. 2020;.

[12] Hirotsu Y, Maejima M, Shibusawa M, Nagakubo Y, Hosaka K, Amemiya K et al. Comparison of automated SARS-CoV-2 antigen test for COVID-19 infection with quantitative RT-PCR using 313 nasopharyngeal swabs, including from seven serially followed patients. International Journal of Infectious Diseases. 2020;99:397-402.

[13] James A, Gulley T, Kothari A, Holder K, Garner K, Patil N. Performance of the BinaxNOW coronavirus disease 2019 (COVID-19) Antigen Card test relative to the severe acute respiratory coronavirus virus 2 (SARS-CoV-2) real-time reverse transcriptase polymerase chain reaction (rRT-PCR) assay among symptomatic and asymptomatic healthcare employees. Infection Control & Hospital Epidemiology. 2021;:1-3.

[14] Nagura-Ikeda M, Imai K, Tabata S, Miyoshi K, Murahara N, Mizuno T et al. Clinical Evaluation of Self-Collected Saliva by Quantitative Reverse Transcription-PCR (RT-qPCR), Direct RT-qPCR, Reverse Transcription–Loop-Mediated Isothermal Amplification,

and a Rapid Antigen Test To Diagnose COVID-19. Journal of Clinical Microbiology. 2020;58(9).

[15] Krüttgen A, Cornelissen C, Dreher M, Hornef M, Imöhl M, Kleines M. Comparison of the SARS-CoV-2 Rapid antigen test to the real star Sars-CoV-2 RT PCR kit. Journal of Virological Methods. 2021;288:114024.

[16] Lambert-Niclot S, Cuffel A, Le Pape S, Vauloup-Fellous C, Morand-Joubert L, Roque-Afonso A et al. Evaluation of a Rapid Diagnostic Assay for Detection of SARS-CoV-2 Antigen in Nasopharyngeal Swabs. Journal of Clinical Microbiology. 2020;58(8).

[17] Linares M, Pérez-Tanoira R, Carrero A, Romanyk J, Pérez-García F, Gómez-Herruz P et al. Panbio antigen rapid test is reliable to diagnose SARS-CoV-2 infection in the first 7 days after the onset of symptoms. Journal of Clinical Virology. 2020;133:104659.

[18] Mak G, Cheng P, Lau S, Wong K, Lau C, Lam E et al. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. Journal of Clinical Virology. 2020;129:104500.

[19] Mertens P, De Vos N, Martiny D, Jassoy C, Mirazimi A, Cuypers L et al. Development and Potential Usefulness of the COVID-19 Ag Respi-Strip Diagnostic Assay in a Pandemic Context. Frontiers in Medicine. 2020;7.

[20] Möckel M, Corman V, Stegemann M, Hofmann J, Stein A, Jones T et al. SARS-CoV-2 antigen rapid immunoassay for diagnosis of COVID-19 in the emergency department. Biomarkers. 2021;:1-10.

[21] Nalumansi A, Lutalo T, Kayiwa J, Watera C, Balinandi S, Kiconco J et al. Field evaluation of the performance of a SARS-CoV-2 antigen rapid diagnostic test in Uganda using nasopharyngeal samples. International Journal of Infectious Diseases. 2021;104:282-286.

[22] Osterman A, Baldauf H, Eletreby M, Wettengel J, Afridi S, Fuchs T et al. Evaluation of two rapid antigen tests to detect SARS-CoV-2 in a hospital setting. Medical Microbiology and Immunology. 2021;.

[23] Pilarowski G, Marquez C, Rubio L, Peng J, Martinez J, Black D et al. Field performance and public health response using the BinaxNOW TM Rapid SARS-CoV-2 antigen detection assay during community-based testing. Clinical Infectious Diseases. 2020;.

[24] Porte L, Legarraga P, Vollrath V, Aguilera X, Munita J, Araos R et al. Evaluation of a novel antigen-based rapid detection test for the diagnosis of SARS-CoV-2 in respiratory samples. International Journal of Infectious Diseases. 2020;99:328-333.

[25] Pray IW, Ford L, Cole D, et al. Performance of an Antigen-Based Test for Asymptomatic and Symptomatic SARS-CoV-2 Testing at Two University Campuses — Wisconsin, September–October 2020. MMWR Morb Mortal Wkly Rep 2021;69:1642–1647. DOI: http://dx.doi.org/10.15585/mmwr.mm695152a3external icon.

[26] Prince-Guerra J, Almendares O, Nolen L, Gunn J, Dale A, Buono S et al. Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 Infection at Two Community-Based Testing Sites — Pima County, Arizona, November 3–17, 2020. MMWR Morbidity and Mortality Weekly Report. 2021;70(3):100-105.

[27] Rottenstreich A, Zarbiv G, Kabiri D, Porat S, Sompolinsky Y, Reubinoff B et al. Rapid antigen detection testing for universal screening for severe acute respiratory syndrome coronavirus 2 in women admitted for delivery. American Journal of Obstetrics and Gynecology. 2021;.

[28] Scohy A, Anantharajah A, Bodéus M, Kabamba-Mukadi B, Verroken A, Rodriguez-Villalobos H. Low performance of rapid antigen detection test as frontline testing for COVID-19 diagnosis. Journal of Clinical Virology. 2020;129:104455.

[29] Torres I, Poujois S, Albert E, Colomina J, Navarro D. Evaluation of a rapid antigen test (Panbio™ COVID-19 Ag rapid test device) for SARS-CoV-2 detection in asymptomatic close contacts of COVID-19 patients. Clinical Microbiology and Infection. 2021;.

[30] Turcato G, Zaboli A, Pfeifer N, Ciccariello L, Sibilio S, Tezza G et al. Clinical application of a rapid antigen test for the detection of SARS-CoV-2 infection in symptomatic and asymptomatic patients evaluated in the emergency department: A preliminary report. Journal of Infection 2020

[31] Weitzel T, Legarraga P, Iruretagoyena M, Pizarro G, Vollrath V, Araos R et al. Comparative evaluation of four rapid SARS-CoV-2 antigen detection tests using universal transport medium. Travel Medicine and Infectious Disease. 2021;39:101942.

[32] Young S, Taylor S, Cammarata C, Varnado K, Roger-Dalbert C, Montano A et al. Clinical Evaluation of BD Veritor SARS-CoV-2 Point-of-Care Test Performance Compared to PCR-Based Testing and versus the Sofia 2 SARS Antigen Point-of-Care Test. Journal of Clinical Microbiology. 2020;59(1).

[33] FIND Evaluation of Abbott Panbio COVID-19 Ag Rapid Test Device External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2020/12/Panbio_Ag-Public-Report_v2.1.pdf CD

[34] FIND Evaluation of Abbott Panbio COVID-19 Ag Rapid Test Device (NASAL) External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2021/02/Panbio_Nasal_Ag-Public-Report_20210211v1.pdf E

[35] FIND Evaluation of Bionote, Inc. NowCheck COVID-19 Ag Test External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2020/12/Bionote_Ag-INTERIM-Public-Report_20201210-v1-4.pdf G

[36] FIND Evaluation of Coris BioConcept COVID-19 Ag Respi-Strip External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2020/12/Coris-RespiStrip-Ag_Public-Report_20201210-v1-2.pdf H

[37] FIND Evaluation of Joysbio (Tianjin) Biotechnology Co., Ltd. SARS-CoV-2 Antigen Rapid Test Kit (Colloidal Gold) External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2021/02/Joysbio_Ag-Public-Report_v1_20210211.pdf I

[38] FIND Evaluation of RapiGEN Inc. BIOCREDIT COVID-19 Ag External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2020/12/Rapigen_Ag-Public-Report_20201210-v2-1.pdf JK

[39] FIND Evaluation of SD Biosensor, Inc. STANDARD™ F COVID-19 Ag FIA External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2020/12/STANDARD_F_Ag-Public-Report_20201210-v2-1.pdf AB

[40] FIND Evaluation of SD Biosensor, Inc. STANDARD Q COVID-19 Ag Test External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2020/12/SDQ-Ag-Public-Report_20201210-v2-1.pdf LMN

[41] FIND Evaluation of SD Biosensor, Inc. STANDARD Q COVID-19 Ag Test, nasal swab External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2021/01/SDQ_Nasal_Ag-Public-Report_20210119v1.pdf O

[42] FIND Evaluation of Shenzhen Bioeasy Biotechnology Co. Ltd. 2019-nCoV Ag Rapid Test Kit (Fluorescence) External Report [Internet]. Finddx.org. 2021 [cited 19 February 2021]. Available from: https://www.finddx.org/wp-content/uploads/2021/01/Bioeasy-Ag_Public-Report_20210119-V1.0.pdf Q

[43] Interim Guidance for Antigen Testing for SARS-CoV-2 [Internet]. Centers for Disease Control and Prevention. 2021 [cited 19 February 2021]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html

[44] Rapid Testing [Internet]. Idsociety.org. 2021 [cited 19 February 2021]. Available from: https://www.idsociety.org/covid-19-real-time-learning-network/diagnostics/rapid-testing/

[45] Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19 [Internet]. Idsociety.org. 2021 [cited 19 February 2021]. Available from: https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/

[46] Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays [Internet]. Who.int. 2021 [cited 19 February 2021]. Available from: https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays

Appendix 1. Characteristics of Included Studies

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
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)
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%) Unknown (n = 17, 11%)	148	Genesig® Real-Time PCR assay (Primerdesign Ltd., Chander´s Ford, UK)	Nasopharyngeal swab

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
				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
Albert 2020	Spain	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal	Clinically suspected with COVID-19, symptomatic	412	TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, MS, USA	Nasopharyngeal swab
Cerutti 2020	Italy	STANDARD Q COVID19 Ag (SD-Biosensor)	Nasopharyngeal	suspect of COVID-19 (185) and travelers returning home from high risk countries (145)	330	1) Seegene Allplex® 2019 n-CoV Assay (N = 159) 2) DiaSorin Simplexa® (n = 28) 3) Cobas 6800 Roche® (N = 118)	Nasopharyngeal swab
Chaimayo 2020	Bangkok, Thailand	STANDARD Q COVID19 Ag (SD-Biosensor)	mainly nasopharyngeal and throat swabs A total of 454 respiratory samples, including 447 nasopharyngeal (NP) and throat swabs, four endotracheal aspirates (tracheal suctions), and three sputum samples, were collected from suspected COVID-19 cases	COVID-19 suspected cases and contact individuals, including pre-operative patients	454	Allplex 2019-nCoV Assay (Seegene, Korea)	nasopharyngeal and throat swabs
Ciotti 2021	Italy	Coris Coronavirus Disease 2019 Ag Respi-Strip test	nasopharyngeal swabs	suspected cases of SARS-CoV-2 infection	50	Allplex 2019-nCoV Assay (Seegene, Korea)	nasopharyngeal swabs
Favresse 2021 (A)	Belgium	Biotical SARS-CoV-2 Ag	Nasopharyngeal	One hundred and eighteen (62.8%) were symptomatic patients, and 70 (37.2%) were asymptomatic subjects.	188	LightCycler® (Roche Diagnostics®, Basel, Switzerland)) 480 Instrument II (Roche Diagnostics®) using the LightMix® (Roche	nasopharyngeal swabs

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
						Diagnostics®) Modular SARS-CoV E-gene set	
Favresse 2021 (B)	Belgium	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal	One hundred and eighteen (62.8%) were symptomatic patients, and 70 (37.2%) were asymptomatic subjects.	188	LightCycler® (Roche Diagnostics®, Basel, Switzerland)) 480 Instrument II (Roche Diagnostics®) using the LightMix® (Roche Diagnostics®) Modular SARS-CoV E-gene set	nasopharyngeal swabs
Favresse 2021 (C)	Belgium	Healgen Coronavirus Ag Rapid Test	Nasopharyngeal	One hundred and eighteen (62.8%) were symptomatic patients, and 70 (37.2%) were asymptomatic subjects.	188	LightCycler® (Roche Diagnostics®, Basel, Switzerland)) 480 Instrument II (Roche Diagnostics®) using the LightMix® (Roche Diagnostics®) Modular SARS-CoV E-gene set	nasopharyngeal swabs
Favresse 2021 (D)	Belgium	Roche SARS-CoV-2 Rapid Antigen Test	Nasopharyngeal	One hundred and eighteen (62.8%) were symptomatic patients, and 70 (37.2%) were asymptomatic subjects.	188	LightCycler® (Roche Diagnostics®, Basel, Switzerland)) 480 Instrument II (Roche Diagnostics®) using the LightMix® (Roche Diagnostics®) Modular SARS-CoV E-gene set	nasopharyngeal swabs
Favresse 2021 (E)	Belgium	VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test	Nasopharyngeal	One hundred and eighteen (62.8%) were symptomatic patients, and 70 (37.2%) were asymptomatic subjects.	188	LightCycler® (Roche Diagnostics®, Basel, Switzerland)) 480 Instrument II (Roche Diagnostics®) using the LightMix® (Roche Diagnostics®) Modular SARS-CoV E-gene set	nasopharyngeal swabs
Gremmels 2021 (A)	Netherlands	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal	community-dwelling mildly symptomatic subjects	1369	Allplex 19-nCoV multiplex platform for detection of SARS-CoV-2 (Seegene, South-Korea),	nasopharyngeal and throat swabs
Gremmels 2021 (B)	Aruba	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal	community-dwelling mildly symptomatic subjects	208	Allplex 19-nCoV multiplex platform for detection of SARS-CoV-2 (Seegene, South-Korea),	nasopharyngeal and throat swabs
Hirotsu 2020	Japan	LUMIPULSE SARS-CoV-2 Ag	nasopharyngeal	individuals at Yamanashi Central Hospital	313	TaqMan Fast Virus 1-Step Master Mix (Thermo Fisher Scientific); StepOnePlus Real-Time PCR System (Thermo Fisher Scientific)	nasopharyngeal swabs
James 2021 (A)	USA	BinaxNOW COVID-19 Ag Card test kit	Nasopharyngeal	Symptomatic	115	PerkinElmer SARS-CoV-2 real-time RT-PCR assay	nasal swab

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
		(Abbott Diagnostics, Scarborough, ME)					
James 2021 (B)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	Nasopharyngeal	Asymptomatic	2224	PerkinElmer SARS-CoV-2 real-time RT-PCR assay	nasal swab
Kruttgen 2020	Germany	Roche SARS-CoV-2 Rapid Antigen Test	Nasopharyngeal	Unknown	150	Real Star SARS-CoV 2 RT PCR Kit (Altona, Germany)	nasopharyngeal swabs
Linares 2020	Spain	Panbio COVID-19 Ag Rapid Test	nasopharyngeal samples	Mixed	255	Allplex SARS-CoV-2 assay (Seegene, Seoul, South Korea)	nasopharyngeal swabs
Mockel 2021	Germany	Roche SARS-CoV-2 Rapid Antigen Test	oro-nasopharyngeal swabs	Symptomatic - Acute respiratory symptoms and/or loss of smell or taste. - Contact with a confirmed COVID-19 case up to a maximum of 14 days before onset of any COVID-19 symptoms (cough, fever, rhinorrhea, sore throat, dyspnea, headache, muscle ache, loss of appetite, loss of body weight, nausea, abdominal pain, vomiting, diarrhea, conjunctivitis, skin efflorescence, lymphadenopathy, apathy, or somnolence). - Clinical or radiological signs of viral pneumonia in the context of an outbreak in nursing homes or hospitals.	483	Roche cobas SARS-CoV-2 assay (Penzberg, Germany) on the Roche cobas® 6800 or 8800 system or the Roche MagNA Pure 96 System for RNA purification and the SARS-CoV-2 E-gene assay from TibMolbiol (Berlin, Germany)	nasopharyngeal swabs
Nalumansi 2020	Uganda	STANDARD Q COVID19 Ag (SD-Biosensor)	nasopharyngeal samples	suspected COVID-19 cases and low-risk volunteers	262	viral RNA mini kit (QIAGEN, Hilden, Germany); qRT-PCR (Berlin Protocol)	nasal swabs
Osterman 2021 (A)	Germany	STANDARD™ F COVID-19 Ag FIA (FIA) SD Biosensor	(nasopharygeal or oropharyngeal)	asymptomatic and symptomatic patients and health care workers	767	the nucleocapsid (N1) reac-tion (Center for Disease Control (CDC) protocol [1], the envelope amplification (Charité protocol [2, 6]), the nucle-ocapsid amplification (Seegene Allplex 2019-nCoV Assay), the Roche Cobas SARS-CoV-2 nucleocapsid reaction or the	respiratory swabs (nasopharygeal or oropharyngeal)

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
						Xpert Xpress SARS-CoV-2 run on the GeneXpert System	
Osterman 2021 (B)	Germany	Roche SARS-CoV-2 Rapid Antigen Test	(nasopharygeal or oropharyngeal)	asymptomatic and symptomatic patients and health care workers	66	Real Accurate Quadruplex SARS CoV-2 PCR Kit, detecting the N gene and RdRp gene and including an inhibi- tory control (Pathofinder, Maastricht, Netherlands) run on a Taqman 7500 (Thermo Fisher Scientific, Waltham, USA), and the Xpert Xpress SARS-CoV-2 run on the GeneXpert System.	nasopharyngeal swabs
Pilarowski 2020 (A)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	bilateral anterior nasal swab	with or without symptoms,	3302	Renegade Bio using RenegadeXP technology	Anterior nares
Pilarowski 2020 (B)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	bilateral anterior nasal swab	with or without symptoms,	3302	Renegade Bio using RenegadeXP technology	Anterior nares
Pilarowski 2020 (C)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	bilateral anterior nasal swab	Symptoms	671	SARS-COV-2 RT PCR	Anterior nares
Pilarowski 2020 (D)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	bilateral anterior nasal swab	Symptoms	671	SARS-COV-2 RT PCR	Anterior nares
Pilarowski 2020 (E)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	sequential anterior swab (both nares per swab)	Asymptomatic	871	SARS-COV-2 RT PCR	Anterior nares
Pray 2021 (A)	USA	Sofia SARS Antigen Fluorescent Immunoassay testing	Paired nasal swabs	Symptomatic	227	CDC 2019-nCoV real-time RT-PCR diagnostic panel	nasal swabs
Pray 2021 (B)	USA	Sofia SARS Antigen Fluorescent Immunoassay testing	Paired nasal swabs	Asymptomatic	871	TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific)	nasal swabs
Prince-Guerra 2021 (A)	USA	BinaxNOW COVID-19 Ag Card test kit	Anterior nasal swabs	Symptomatic	1458	1) CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel for detection of SARS-CoV-2	bilateral nasopharyngeal swab

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
		(Abbott Diagnostics, Scarborough, ME)				(2,582 swabs) 2) Fosun COVID-19 RT-PCR Detection Kit (837 swabs)	
Prince-Guerra 2021 (B)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	Anterior nasal swabs	Asymptomatic	1458	1) CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel for detection of SARS-CoV-2 (2,582 swabs) 2) Fosun COVID-19 RT-PCR Detection Kit (837 swabs)	bilateral nasopharyngeal swab
Prince-Guerra 2021 (C)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	Anterior nasal swabs	Symptomatic	1961	1) CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel for detection of SARS-CoV-2 (2,582 swabs) 2) Fosun COVID-19 RT-PCR Detection Kit (837 swabs)	bilateral nasopharyngeal swab
Prince-Guerra 2021 (D)	USA	BinaxNOW COVID-19 Ag Card test kit (Abbott Diagnostics, Scarborough, ME)	Anterior nasal swabs	Symptomatic	1961	1) CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel for detection of SARS-CoV-2 (2,582 swabs) 2) Fosun COVID-19 RT-PCR Detection Kit (837 swabs)	bilateral nasopharyngeal swab
Rottenstreich 2021	Israel	NowCheck COVID-19 Ag Test Bionote Inc	Nasopharyngeal	asymptomatic women admitted for delivery	1326	SARS-CoV-2 using RT-PCR	nasopharyngeal swabs
Torres 2021	Spain	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal	asymptomatic individuals	634	TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, MA, USA)	nasopharyngeal swabs
Turcato 2020 (A)	Italy	STANDARD Q COVID19 Ag (SD-Biosensor)	Nasopharyngeal	Symptomatic	991	SARS-CoV-2 RT PCR	nasopharyngeal swabs
Turcato 2020 (B)	Italy	STANDARD Q COVID19 Ag (SD-Biosensor)	Nasopharyngeal	Asymptomatic	2419	SARS-CoV-2 RT PCR	nasopharyngeal swabs
Young 2020	USA	BD Veritor System (Veritor)	either nasopharyngeal or oropharyngeal specimens	Symptomatic	260	Lyra SARS-CoV-2 PCR assay (Lyra)	either nasopharyngeal or oropharyngeal specimens
Agullo 2020a	Spain	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal	Unknown	652	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agullo 2020b	Spain	Panbio COVID-19 Ag Rapid Test	Anterior Nares	Unknown	659	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agullo 2020c	Spain	Panbio COVID-19 Ag Rapid Test	Saliva Sample	Unknown	610	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
Agullo 2020d	Spain	Panbio COVID-19 Ag Rapid Test	Nasal and anterior Nares	Unknown	610	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agullo 2020e	Spain	Panbio COVID-19 Ag Rapid Test	Anterior Nares	Unknown	394	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agullo 2020f	Spain	Panbio COVID-19 Ag Rapid Test	Anterior Nares	Unknown	265	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agullo 2020g	Spain	Panbio COVID-19 Ag Rapid Test	Saliva Sample	Unknown	366	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agullo 2020h	Spain	Panbio COVID-19 Ag Rapid Test	Saliva Sample	Unknown	244	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agulla 2020o	Spain	Panbio COVID-19 Ag Rapid Test	Nasal and anterior Nares	Unknown	369	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
Agulla 2020o	Spain	Panbio COVID-19 Ag Rapid Test	Nasal and anterior Nares	Unknown	245	Cobas z 480 Analyzer (Roche, Basilea, Suiza)	nasopharyngeal swabs
FindDx A	Brazil	STANDARD™ F COVID-19 Ag FIA (FIA) SD Biosensor	Nasopharyngeal swab	Adults in community meeting national suspect definition	453	Lab-developed assay based on the US CDC protocol, which targets two regions (N1 and N2) of the nucleocapsid (N) gene of SARS-CoV-2; Lab-developed assay based on the Charité Universitätsmedizin Berlin protocol, which has 2 gene targets (E and RdRp) of SARS-CoV-2	Nasopharyngeal swab
FindDx B	Germany	STANDARD™ F COVID-19 Ag FIA (FIA) SD Biosensor	1. HD: Nasopharyngeal swabs 2. Berlin: Combined naso- /oropharyngeal swab	Adults able to ambulate and meeting suspect definition of the Department of public health	676	Cobas SARS-CoV-2 (Roche Diagnostics Inc) o N = 342 • Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) o N = 1 Allplex 2019-nCov Assay (Seegene Inc) o N = 20 • LightMix® Modular SARS-CoV (COVID19) E-gene (Tib Molbiol) o N = 233 • Cobas (Roche) or Thermofisher (Multiplex TaqPath COVID-19 CE-IVD RT-PCR Kit) o N = 80	Nasopharyngeal (n=305), Naso/oropharyngeal (n=342) and/or Oropharyngeal swabs (n=32)

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
FindDx C	Switzerland	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal swab	Adults in community meeting Department of Public Health definition of a suspected COVID-19 case and being tested for SARS-CoV-2 part of routine medical care.	535	Cobas SARS-CoV-2 (Roche Diagnostics Inc)	Nasopharyngeal swab
FindDx D	Germany	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal	Adults able to ambulate and meeting suspect definition of the Department of public health	1108	• Allplex 2019-nCov Assay (Seegene Inc) o N = 725 • LightMix® Modular SARSCoV (COVID19) E-gene (Tib Molbiol) o N = 15 • RealStar® SARS-CoV-2 RT-PCR Kit (altona Diagnostics) o N = 88	Nasopharyngeal swab
FindDx E	Germany	Panbio COVID-19 Ag Rapid Test	Nasal Swab	Adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting suspect definition of the Department of Public Health	281	• LightMix® Modular SARS-CoV (COVID19) Egene (Tib Molbiol) o N = 266 • Allplex 2019-nCov Assay (Seegene Inc) o N = 13 • Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) o N = 3	Nasopharyngeal (NP)
FindDx F	Germany	Panbio COVID-19 Ag Rapid Test	Nasopharyngeal swab	Adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting suspect definition of the Department of Public Health	281	• LightMix® Modular SARS-CoV (COVID19) Egene (Tib Molbiol) o N = 266 • Allplex 2019-nCov Assay (Seegene Inc) o N = 13 • Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) o N = 3	Nasopharyngeal (NP)
FindDx G	Brazil	NowCheck COVID-19 Ag Test Bionote Inc	NP swab	Adults in community meeting national suspect definition	400	Lab-developed assay based on the US CDC protocol, which targets two regions (N1 and N2) of the nucleocapsid (N) gene of SARS-CoV-2	Nasopharyngeal swabs
FindDx H	Germany and UK	Coris Coronavirus Disease 2019 Ag Respi-Strip test	1. HD: Nasopharyngeal swabs 2. Berlin: Combined naso-/oropharyngeal swab 3. Liverpool: Combined naso-/oropharyngeal swab	1. Germany and Berlin: Adults able to ambulate and meeting suspect definition of the Department of public health. Provided informed consent 2. Liverpool: Adults admitted to LUHFT suspected to have COVID-19 with following symptoms: fever ≥ 37.8C +/- shortness of breath +/- new persistent cough +/- loss of smell OR clinical or radiological evidence of pneumonia. Provided informed consent.	425	• Allplex 2019-nCov Assay (Seegene Inc) • Cobas SARS-CoV-2 (Roche Diagnostics Inc) • genesig® COVID-19 Real-Time PCR Assay (Primerdesign, Ltd.) • LightMix® Modular SARS-CoV (COVID19) E-gene (Tib Molbiol)	naso/oropharyngeal swabs

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
FindDx I	Switzerland	SARS-CoV-2 Antigen Rapid Test Kit (Colloidal Gold)	Anterior Nares (AN, Nasal) swab	Adults in community meeting Department of Public Health definition of a suspected COVID-19 case and being tested for SARS-CoV-2 part of routine medical care.	265	Cobas SARS-CoV-2 (Roche Diagnostics Inc) (n=216) Xpert Xpress SARS-CoV-2 (Cepheid) (n=1) TaqPath™ COVID-19 CE IVD RT PCR Kit (Thermo Fisher Scientific) (with Nimbus Presto Extraction instrument) (n=48)	Nasopharyngeal swab
FindDx J	Brazil	BIOCREDIT COVID-19 Ag test	Nasopharyngeal swab	Adults in community meeting national suspect definition	476	Lab-developed assay based on the US CDC protocol, which targets two regions (N1 and N2) of the nucleocapsid (N) gene of SARS-CoV-2	Nasopharyngeal (NP) swab
FindDx K	Germany	BIOCREDIT COVID-19 Ag test	NP/OR	Adults able to ambulate and meeting suspect definition of the Department of public health	1239	Cobas SARS-CoV-2 (Roche Diagnostics Inc) o N = 344 • Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) o N = 114 • Allplex 2019-nCov Assay (Seegene Inc) o N = 571	Nasopharyngeal (NP, n=843), Naso/oropharyngeal (NP/OP, n=276), or oropharyngeal (OP, n=131) swabs
FindDx L	Brazil	STANDARD Q COVID19 Ag (SD-Biosensor)	1. HD: Nasopharyngeal swabs 2. Berlin: Combined naso- /oropharyngeal swab	Adults able to ambulate and meeting suspect definition of the Department of public health	400	Cobas SARS-CoV-2 (Roche Diagnostics Inc) o N = 912 Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc) o N = 78 • Genesig COVID-19 Real-Time PCR assay (Primerdesign, Inc) o N = 19 • Allplex 2019-nCov Assay (Seegene Inc) o N = 125 • LightMix® Modular SARS-CoV (COVID19) E-gene (Tib Molbiol) o N = 131	Naso/oropharyngeal swabs
FindDx M	Germany	STANDARD Q COVID19 Ag (SD-Biosensor)	Nasopharyngeal swabs	Adults in community meeting national suspect definition	1263	Lab-developed assay based on the US CDC protocol, which targets two regions (N1 and N2) of the nucleocapsid (N) gene of SARSCoV-2	Nasopharyngeal swabs
FindDx N	Switzerland	STANDARD Q COVID19 Ag (SD-Biosensor)	Nasopharyngeal swabs	Adults in community meeting Department of Public Health definition of a suspected COVID19 case and being tested for SARS-CoV-2 part of routine medical care.	529	Cobas SARS-CoV-2 (Roche Diagnostics Inc)	Nasopharyngeal swabs
FindDx O	Germany	STANDARD Q COVID19 Ag (SD-Biosensor)	Nasal swab	Adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting	179	Cobas SARS-CoV-2 (Roche Diagnostics Inc) o N = 158 • LightMix® Modular SARS-CoV	Nasopharyngeal (NP)

Study ID	Setting	Index Test	Index Test Specimen	Population	Sample Size	Reference standard	Reference Standard Specimen
				suspect definition of the Department of Public Health		(COVID19) Egene (Tib Molbiol)	
FindDx P	Germany	STANDARD Q COVID19 Ag (SD-Biosensor)	Nasopharyngeal swab	Adults able to ambulate, at high risk for SARS-CoV-2 according to clinical suspicion, and meeting suspect definition of the Department of Public Health	179	Cobas SARS-CoV-2 (Roche Diagnostics Inc) o N = 158 • LightMix® Modular SARS-CoV (COVID19) Egene (Tib Molbiol) o N = 21	Nasopharyngeal (NP)
FindDx Q	Germany	Bioeasy 2019-nCoV Ag Fluorescence Rapid Test Kit	1. HD: Nasopharyngeal swab (or oropharyngeal swabs if NP was contra-indicated) 2. Berlin: Combined Naso/oropharyngeal swabs	Heidelberg and Berlin: Adults able to ambulate and meeting suspect definition of the Department of public health	729	Cobas SARS-CoV-2 (Roche Diagnostics Inc); o n = 223 Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc); o n = 5 • Allplex 2019-nCov Assay (Seegene Inc); o n = 343 • LightMix® Modular SARS-CoV (COVID19) Egene (Tib Molbiol); o n = 158	HD: nasopharyngeal (NP) swabs (or oropharyngeal swabs if NP was contra-indicated) 2. Berlin: combined naso/oropharyngeal swabs

Appendix 2: GRADE Evidence Profile

Question: Should rapid antigen test alone (using nasopharyngeal specimen) be used to diagnose COVID-19 in patients suspected with COVID-19?

Sensitivity	0.72 (95% CI: 0.65 to 0.78)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	36 studies 1080 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	36 (33 to 39)	72 (65 to 78)	144 (130 to 156)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								14 (11 to 17)	28 (22 to 35)	56 (44 to 70)	
True negatives (patients without COVID-19)	36 studies 1080 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	950 (941 to 950)	900 (891 to 900)	800 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 8)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone (using naso- and oropharyngeal specimen) be used to diagnose COVID-19 in patients suspected with COVID-19?

Sensitivity	0.65 (95% CI: 0.47 to 0.79)
Specificity	0.99 (95% CI: 0.97 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	16 studies 65 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	33 (24 to 40)	65 (47 to 79)	130 (94 to 158)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								17 (10 to 26)	35 (21 to 53)	70 (42 to 106)	
True negatives (patients without COVID-19)	0 studies patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	941 (922 to 950)	891 (873 to 900)	792 (776 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								9 (0 to 28)	9 (0 to 27)	8 (0 to 24)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone (using saliva specimen) be used to diagnose COVID-19 in patients suspected with COVID-19?

Sensitivity	0.17 (95% CI: 0.13 to 0.23)
Specificity	0.99 (95% CI: 0.97 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	2 studies 762 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	9 (7 to 12)	17 (13 to 23)	34 (26 to 46)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								41 (38 to 43)	83 (77 to 87)	166 (154 to 174)	
True negatives (patients without COVID-19)	2 studies 762 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	941 (922 to 950)	891 (873 to 900)	792 (776 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								9 (0 to 28)	9 (0 to 27)	8 (0 to 24)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone (using anterior nares specimen) be used to diagnose COVID-19 in patients suspected with COVID-19?

Sensitivity	0.84 (95% CI: 0.66 to 0.93)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	15 studies 2004 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	42 (33 to 47)	84 (66 to 93)	168 (132 to 186)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								8 (3 to 17)	16 (7 to 34)	32 (14 to 68)	
True negatives (patients without COVID-19)	15 studies 2004 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	950 (941 to 950)	900 (891 to 900)	800 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 8)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone be used to diagnose COVID-19 in asymptomatic patients suspected with COVID-19?

Sensitivity	0.51 (95% CI: 0.39 to 0.63)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	7.8%	10%	20%

Outcome	№ of studies (№ of patients)	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 7.8%	pre-test probability of 10%	pre-test probability of 20%	
True positives (patients with COVID-19)	7 studies 10937 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	40 (30 to 49)	51 (39 to 63)	102 (78 to 126)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								38 (29 to 48)	49 (37 to 61)	98 (74 to 122)	
True negatives (patients without COVID-19)	7 studies 10937 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	922 (913 to 922)	900 (891 to 900)	800 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 8)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone be used to diagnose COVID-19 in patients suspected with COVID-19 regardless whether they are symptomatic or asymptomatic?

Sensitivity	0.67 (95% CI: 0.57 to 0.77)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	32 studies 8964 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	34 (28 to 39)	67 (57 to 77)	134 (114 to 154)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								16 (11 to 22)	33 (23 to 43)	66 (46 to 86)	
True negatives (patients without COVID-19)	32 studies 8964 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	950 (941 to 950)	900 (891 to 900)	800 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 8)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone be used to diagnose COVID-19 in patients who are either in the early or late phase of the disease?

Sensitivity	0.81 (95% CI: 0.76 to 0.85)
Specificity	0.99 (95% CI: 0.98 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	16 studies 2698 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	41 (38 to 43)	81 (76 to 85)	162 (152 to 170)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								9 (7 to 12)	19 (15 to 24)	38 (30 to 48)	
True negatives (patients without COVID-19)	16 studies 2698 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	941 (931 to 950)	891 (882 to 900)	792 (784 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								9 (0 to 19)	9 (0 to 18)	8 (0 to 16)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone be used to diagnose COVID-19 in patients with unknown phase of the disease?

Sensitivity	0.68 (95% CI: 0.57 to 0.77)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	40 studies 5760 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	34 (28 to 39)	68 (57 to 77)	136 (114 to 154)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								16 (11 to 22)	32 (23 to 43)	64 (46 to 86)	
True negatives (patients without COVID-19)	40 studies 5760 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	950 (941 to 950)	900 (891 to 900)	800 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 8)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone be used to diagnose COVID-19 in patients within the early phase of the disease (i.e., 0 to 7 days)?

Sensitivity	0.71 (95% CI: 0.44 to 0.89)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	12 studies 2912 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	36 (22 to 45)	71 (44 to 89)	142 (88 to 178)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								14 (5 to 28)	29 (11 to 56)	58 (22 to 112)	
True negatives (patients without COVID-19)	12 studies 2912 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	950 (941 to 950)	900 (891 to 900)	800 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 8)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone be used to diagnose COVID-19 in patients within the late phase of the disease (i.e., 8 to 14 days)?

Sensitivity	0.65 (95% CI: 0.57 to 0.71)
Specificity	0.99 (95% CI: 0.99 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	2 studies 831 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	33 (28 to 36)	65 (57 to 71)	130 (114 to 142)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								17 (14 to 22)	35 (29 to 43)	70 (58 to 86)	
True negatives (patients without COVID-19)	2 studies 831 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	941 (941 to 950)	891 (891 to 900)	792 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								9 (0 to 9)	9 (0 to 9)	8 (0 to 8)	

Explanations

a. Rated down for population indirectness

Question: Should rapid antigen test alone be used to diagnose COVID-19 in symptomatic patients suspected with COVID-19?

Sensitivity	0.78 (95% CI: 0.69 to 0.86)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	5%	10%	20%

Outcome	№ of studies (№ of patients)	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)	30 studies 12559 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	39 (34 to 43)	78 (69 to 86)	156 (138 to 172)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having COVID-19)								11 (7 to 16)	22 (14 to 31)	44 (28 to 62)	
True negatives (patients without COVID-19)	30 studies 12559 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	950 (941 to 950)	900 (891 to 900)	800 (792 to 800)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having COVID-19)								0 (0 to 9)	0 (0 to 9)	0 (0 to 8)	

Explanations

a. Rated down for population indirectness

Appendix 3: Characteristics of Ongoing Studies (n = 10)

NCT Number	Title	Interventions	Outcome Measures
NCT04733170	Clinical Performance Evaluation of KnowNow SARS-CoV-2 Test for the Detection of COVID-19 Antigen	Diagnostic Test: KnowNow SARS-CoV-2 Rapid Antigen Test	Assess clinical diagnostic performance of the KnowNow SARS-CoV-2 Rapid Antigen Test|Efficacy to assess the test compared to the reference test method|Safety and potential risks|Usability Questionnaire to evaluate the use of the test with 2 saliva collection methods
NCT04698993	DrÃ¤ger COVID-19 Antigen Test Clinical Performance Study	Diagnostic Test: DrÃ¤ger Antigen Test SARS-CoV-2	Sensitivity|Specificity|Ease of use|Relationship between DrÃ¤ger test result and specimen viral load|Relationship between DrÃ¤ger test result and time since symptom onset
NCT04689399	Sensitivity and Specificity of SARS-CoV-2 Rapid Antigen Test Compared to RT-PCR Test	Diagnostic Test: Standard Q COVID-19 Ag - test, produced by SD Biosensor INC.	Sensitivity and specificity of the rapid antigen test of COVID-19|Economic analyses|PCR analysis on nasopharyngeal swabs
NCT04682132	Polk COVID-19 and Flu Response	Diagnostic Test: COVID-19 antigen and antibody tests, and influenza rapid test	Prevalence of COVID-19 amongst county emergency personnel|Correlation of common COVID-19 symptoms with result of COVID-19 test|Co-existence of influenza and COVID-19 positive test results
NCT04667442	Investigational Performance Evaluation of the Nanomix eLabÂ® COVID-19 Rapid Antigen Panel With Samples From COVID-19 Positive and Negative Human Subjects	Diagnostic Test: Nanomix eLabÂ® COVID-19 Rapid Antigen Panel (non-interventional)	Demonstrate clinical agreement between an EUA RT-PCR methodology and the Nanomix eLabÂ® COVID-19 Rapid Antigen Panel
NCT04665193	An Approach to Screening for COVID-19 at Vancouver Airport	Diagnostic Test: Rapid Antigen Test	COVID-19 status
NCT04625257	COVID-19 in Baselland: Validation of Simple and Accurate Tests for COVID-19 Detection, Monitoring and Tracing (ACCURATE-BL-COVID-19)	Other: Saliva based assay: crude RNA extraction|Other: Validation of the NGS method|Other: Validation of the LAMP assays|Other: Validation of the POCT Antigen tests	qualitative method validation of the crude extraction in combination with the LAMP or the NGS (count values for detection)
NCT04610489	Diagnostic Performance of an Antigen Test for SARS-CoV-2 Infection (COVID-19)	Diagnostic Test: Quidel Sofia SARS Antigen FIA	Sensitivity|Specificity|Area under the ROC curve
NCT04403906	Somerset and South Essex Coronavirus Antigen Testing	Diagnostic Test: PCL COV05 - COVID 19 Ag Rapid FIA test (Rapid Antigen Test)	To compare the result of SARS-COV2 PCR test to PCL rapid antigen test|Number of technically failed samples due to test issues.|Time taken for PCL Antigen test result
NCT04348864	COVID-19 Diagnostic Self-testing Using Virtual Point-of-care	Diagnostic Test: COVID-19 Antigen/Antibody Rapid Testing, mobile device image capture and telemedicine support|Other: Telemedicine	Clinical accuracy of the antibody and antigen rapid tests compared to LAMP/PCR-based test result|Clinical accuracy of the antibody and antigen rapid tests based on Clinical diagnosis|Self-test interpretation of result vs expert clinical image interpretation of result|Ease of self-testing procedure

Appendix 4. Summary of Ongoing Studies Registered in Finddx.org (n = 8)

Company	Assay	Country of manufacturer	Interpretation	Regulatory status	Evaluation status	Evaluation results
Abbott Rapid Diagnostics	Panbio COVID-19 Ag Test – Nasal	Rep. of Korea	Visual	CE-IVD; WHO EUL	Ongoing	Not yet available
Bionote, Inc.	NowCheck COVID-19 Ag Test – Nasal	Rep. of Korea	Visual	CE-IVD	To start	Not yet available
Boditech Medical, Inc.	iChroma COVID-19 Ag Test	Rep. of Korea	Reader	CE-IVD	Ongoing: 1 country	Not yet available
Edinburgh Genetics, Ltd	ActivXpress+ COVID-19 Antigen Complete Testing Kit	UK	Visual	CE-IVD	Ongoing	Not yet available
Fujirebio Europe N.V.	ESPLINE® SARS-CoV-2	Japan	Visual	CE-IVD	To start	Not yet available
Green Cross Medical Science Corp.	GENEDIA W COVID-19 Ag	Rep. of Korea	Visual	CE-IVD	To start	Not yet available
JOYSBIO (Tianjin) Biotechnology Co., Ltd	SARS CoV 2 Antigen Rapid Test Kit (Colloidal Gold)	China	Visual	CE-IVD	Ongoing: 1 country	Not yet available
Premier Medical Corporation	Sure Status COVID-19 Antigen Card Test	India	Visual	RUO	Ongoing	Not yet available