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

RESEARCH QUESTION: Among patients suspected to have COVID-19, should rapid antigen tests be used for diagnosis of COVID-19?

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Recommendations	Certainty of Evidence	Strength of Recommendation
Among adults and children suspected to have COVID-19 who are symptomatic, we suggest the use of RAT for the diagnosis of COVID-19 as an alternative to RT-PCR.	Very low	Weak
Among adults and children exposed to COVID-19 who are asymptomatic, we suggest against the use of RAT for the diagnosis of COVID-19	Very low	Weak

Consensus Issues

The panel acknowledged that the previous recommendation was updated in the context of the Omicron variant last 2022. The panel emphasized that rapid antigen testing (RAT) is only an alternative to RT-PCR; furthermore, the panel reiterated that the use of RAT in asymptomatic individuals with known exposure to COVID-19 patients is discouraged because of its low sensitivity in this population.

KEY FINDINGS

- We found one systematic review and meta-analysis that included 18 studies done during the Omicron period. The study of Mohammadie et al. reported that overall, rapid antigen tests had a pooled sensitivity of 67% (95% CI 0.59–0.72) and pooled specificity of 100% (0.997–1.000). Subgroup analyses were done with respect to specimen, cycle threshold (CT) value, and symptomatology.

- Nasal swabs had a higher pooled sensitivity of 79% (95% CI 0.69–0.86) compared to nasopharyngeal swabs 67% (95% CI 0.62–0.72). The same finding was reported on the previous version of this review.

- The pooled sensitivity of samples with CT <25 and CT >25 was 90% (95% CI 0.82–0.95) and 11% (95% CI 0.05–0.23), respectively, in a subgroup analysis of seven articles.

- The sensitivity in symptomatic cases was 87% (95% CI 0.81–0.92) while that for asymptomatic cases was 61% (95% CI 0.39–0.79), based on three articles.

WHAT'S NEW IN THIS VERSION?

- This updated review takes into consideration the predominant variant of concern, i.e., Omicron, and focuses on evidence regarding the diagnostic accuracy of rapid antigen tests in the time of Omicron variant predominance.

PREVIOUS RECOMMENDATIONS
As of 22 November 2021

We suggest the use of rapid antigen test for the diagnosis of symptomatic individuals suspected of COVID-19 as an alternative to RT-PCR if all the following conditions are met: *(Low certainty of evidence; Weak recommendation)*

a. Individuals are in the early phase of illness (less than or equal to 7 days from onset of symptoms); AND
b. Testing kits demonstrated sensitivity of more than or equal to 80% AND have very high specificity of more than or equal to 97%.

We suggest the use of rapid antigen tests for the diagnosis of individuals suspected of COVID-19 during the setting of an outbreak provided that all the following conditions are met: *(Very low certainty of evidence; Weak recommendation)*

a. Individuals are in the early phase of illness (less than or equal to 7 days from onset of symptoms); AND
b. Testing kits demonstrated sensitivity of more than or equal to 80% AND have very high specificity of more than or equal to 97%.

We suggest against the use of rapid antigen test for screening purposes. *(Low certainty of evidence; Weak recommendation)*

We suggest against the use of saliva as specimen for rapid antigen test in patients suspected of COVID-19 infection. *(Low certainty of evidence; Weak recommendation)*

We suggest against the use of rapid antigen tests alone in asymptomatic patients suspected of COVID-19 infection*. (Low certainty of evidence; Weak recommendation)*

There is insufficient evidence to recommend for or against the use of repeat antigen testing for screening or diagnosis of COVID-19. *(Very low certainty of evidence)*

A negative rapid antigen test should be confirmed with an RT-PCR in settings or situations wherein COVID-19 is highly suspected (e.g., symptomatic or asymptomatic close contacts of probable or confirmed COVID-19 individuals).

Consensus Issues
The panel was unanimous against (1) the use of rapid antigen test for screening purposes, (2) the use of saliva as specimen for rapid antigen tests, and (3) the use of rapid antigen test alone in asymptomatic patients suspected of COVID-19 infection due to the observed lower sensitivity of these tests under such conditions. A unanimous decision on the insufficiency of evidence to recommend for or against the use of repeat antigen testing was also made.

Majority of the panelists agreed that the following conditions should be met when using rapid antigen tests:

a. Individuals are in the early phase of illness, because antigen tests perform best during this period; and

b. Testing kits have a sensitivity of more than or equal to 80% and specificity of more than or equal to 97%, because the quality of the test kit should be ensured.

One of eleven panelists raised a concern on the specified sensitivity and specificity of the testing kits, as these are based on the Health Technology Assessment Council (HTAC) of the local Department of Health (DOH).

A weak recommendation on the use of rapid antigen tests for diagnosing COVID-19 suspects during outbreaks was made based on nine observational studies with unclear patient selection, conduct of

reference standard, and patient flow and timing. The risk of exposure was an important consideration for the panel, citing that it is not cost-effective to test everyone during an outbreak. However, the risk stratification of participants was not specified in any of the studies

INTRODUCTION

Three years after the emergence of COVID-19, reverse-transcriptase polymerase chain reaction (RT-PCR) still remains the gold standard in diagnosing COVID-19. RT-PCR-based assays have excellent diagnostic accuracy but it has its pitfalls including long turnaround time, high cost, the need for specialized equipment and specialized training of laboratory-based staff. The development of rapid antigen tests has contributed to decreasing the burden on healthcare and lifting restrictions by detecting infected individuals to help prevent further transmission of the virus. Rapid antigen tests (RATs) detect the presence of specific viral antigens that gives fast result, simple to use, requires less training and is less costly compared to RT-PCR [1]. If sufficiently accurate, Ag-RDT can facilitate timely decisions concerning the need for isolation, monitoring, treatment and contact tracing activities [2].

There were several systematic reviews and meta-analyses that assessed the diagnostic accuracy of RAT compared to RT-PCR methods as a reference standard. Majority showed that RAT has high sensitivity and specificity in the early stages of infection, especially when the viral load is high [3]. However, all of these were done before the surge of the Omicron variant.

In the last version of this review done in February 2022, a total of 263 studies were included which spanned all variants of SARS-CoV-2. Only four of these were done, or included patients and tests, in the time of Omicron variant predominance. The review reported that RATs demonstrated a pooled sensitivity of 76% (95% CI 0.52-0.90) and specificity of 100% (95% CI 0.99-1.00) during mass screening. It was also reported that serial testing is more efficient and aids in rapid case detection and contact tracing. RATs use showed a sensitivity of 69% (95% CI 0.49-0.74) and specificity of 99.6% (95% CI 0.98-99) during outbreaks and surges. The sensitivity of rapid antigen tests as part of a testing strategy for travelers still cannot be derived and remains unclear. In children, the pooled sensitivity of rapid antigen testing was shown to be 80% (95% CI 0.72-0.87) and pooled specificity was 99% (95% CI 0.96-0.99).

Taking the evidence from the Omicron studies, a sensitivity of 65% (95% CI 0.60-0.71) and a specificity of 99% (95% CI 0.98-1.00) was reported. Sensitivity was greater than 80% when the test was done using anterior nasal swab samples, when specimens had CT values <30, in symptomatic or asymptomatic patients, and in unvaccinated individuals.

Our latest update considers the newer evidence in light of the Omicron variant which remains the predominant one since its advent in November 2021.

REVIEW METHODS

We searched PubMed, MEDLINE, and Cochrane for published studies from December 2021 using subject headings combined with free text terms related to COVID-19 or SARS-CoV-2 and rapid antigen tests. Search was done from March 15, 2023 to April 4, 2023, using the following search terms: “Rapid Antigen Test”, “Coronavirus”, “Novel Coronavirus”, “Specificity”, “Sensitivity”. We searched for systematic reviews and meta-analyses of studies done when Omicron was the predominant variant of concern. The detailed search can be found in Appendix 1.

A total of 1,003 articles systematic review and meta-analysis of rapid antigen test were found in online databases. After reading the abstracts, 972 articles were removed because they were not aligned with our research questions. Among the 31 articles screened, 6 were discarded, two articles because of duplication and 4 are editorials. The remaining 25 articles were assessed for eligibility and only one

directly fulfilled the eligibility criteria (see Table 1). The 24 systematic reviews excluded were studies done prior to the surge of the Omicron variant. The PRISMA diagram is found in Appendix 2. List of studies screened can be found in Appendix 3.

We considered studies where rapid antigen tests were used in patients suspected to have Omicron variant COVID-19 and compared with RT-PCR for SARS-CoV-2. Studies done prior to the surge of the Omicron variant were excluded.

Critical appraisal and risk of bias assessment was done using AMSTAR-2 (Assessing Methodological Quality of Systematic Review) and Painless Evidence-based Medicine by Dans et al [5,6]. The overall certainty of evidence was assessed using GRADE PRO.

RESULTS

Characteristics of included studies

This updated review includes one systematic review and meta-analysis by Mohammadie et al., which includes 18 articles with 13607 samples from symptomatic and asymptomatic individuals. Of these, 3819 were positive and 9788 were negative for SARS-CoV-2 by RT-PCR. The articles involved one or more brands of the rapid antigen test which was compared to RT-PCR that uses a valid method for viral genotyping. The researchers included only studies that had adequate numbers of clinical specimens from humans suspected to have the Omicron variants of COVID-19. Included in the review were cohort and cross-sectional studies (see Table 2) that were conducted from December 2021 to July 2022, during the surge of the Omicron variant [7].

The population of the studies included both adult and pediatric individuals. There were three studies in the systematic review (Schrom et al , Medoro et al , and Liua et al) that enrolled the pediatric population [8-10].

Relevant Findings

Sensitivity and Specificity of the RAT to Omicron variant

Fifteen of the 18 articles included in the systematic review reported the sensitivity of RAT kits in Omicron cases while 13 articles reported the specificity. Ten articles reported both sensitivity and specificity. The pooled specificity of RATs in this study was 100% [95% CI 0.99–1.00]; the range was 62% [95% CI 0.53–0.71] to 100% [95% CI 0.99– 1.00]. The pooled sensitivity was 67% [95%CI 0.62–0.72], and the range was 22% [95% CI 0.15–0.32] to 100% [95% CI 0.73–1.000]. This is lower than the minimum requirement set by WHO for RAT, which is an overall sensitivity of 80% and specificity 97% [11]. The results of the systematic review revealed a decrease in the sensitivity of RATS in the time of Omicron predominance as compared to the other variants of COVID-19.

Subgroup analysis

Subgroup analyses were performed according to specimen type, symptomatology and viral load.

Specimen type

Subgroup analysis was done on specimen type. Nasal swab had higher pooled sensitivity of 79% [95% CI 0.6–0.86] compared to nasopharyngeal 67% [95% CI 0.62–0.72]. Nasopharyngeal swab is the most commonly used specimen type. The same finding was reported on the previous version of this report.

Symptomatology

Based on symptomatology, the sensitivity in symptomatic 88% [95% CI 0.81–0.92] patients were significantly higher than that in asymptomatic 61% [95% CI 0.39–0.79] cases. This is based on three articles that reported the sensitivity of 210 symptomatic and 143 asymptomatic cases.

Viral load

There is a remarkable difference in sensitivity based on viral load, the pooled sensitivity of samples with CT<5 was 90% [95% CI 0.82–0.95] and CT>25 was 11% [95% CI 0.05–0.23]. This is based on seven articles that reported the sensitivity based on the CT-value (cycle threshold) range of RT-PCR (CT-value<25 and CT-value>25). There is no mention regarding CT value =25.The overall certainty of evidence was rated very low, because of downgrading for inconsistency and risk of bias.

RECOMMENDATIONS FROM OTHER GROUPS

Group or Agency	Recommendation	Date
US FDA [12]	Recommends repeat testing following a negative result, whether you have symptoms or not, to reduce your risk of a false negative test result for suspected Omicron variant	23 March 2023

ONGOING STUDIES AND RESEARCH GAPS

We found no ongoing studies regarding the accuracy of rapid antigen test in diagnosing COVID-19 with Omicron as the variant of concern.

ADDITIONAL CONSIDERATIONS FOR EVIDENCE TO DECISION (ETD) PHASE

The rapid antigen kit costs ₱350-700. This is based on the retail price of these kits in different retail physical and online store. In government agencies, COVID RT-PCR plate-based costs ₱1,200-3,400 for hospital-based and ₱900-5,000 for non-hospital based. COVID RT-PCR cartridge-based costs ₱1,000-3,500 for hospital based while ₱2,450 for non-hospital-based. In private institutions, COVID-RT PCR plate-based costs ₱2,500-4,000 for hospital-based and ₱2,500-3,400 for non-hospital-based. COVID RT-PCR cartridge-based costs ₱3,000-14,000 for hospital-based while ₱3,000-9,000 for non-hospital-based. This data on the price of COVID RT-PCR is based on the DOH website.

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[13] https://doh.gov.ph/covid-19-testing-prices

Appendix 1: Preliminary Evidence to Decision

Table 1. Summary of initial judgements prior to the panel discussion (N=5/9)

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Problem	No	Yes (N=5)					Pitfalls of RTPCR includes long turnaround time, high cost, the need for specialized equipment and specialized training of laboratory-based staff in comparison to RAT detect the presence of specific viral antigens that gives fast result, simple to use, requires less training and is less costly compared to RT-PCR
Benefits	Large (N=4)	Moderate (N=1)	Small	Uncertain			RAT is more affordable, easy to use and with fast results
Harms	Large (N=1)	Moderate (N=2)	Small (N=2)	Uncertain			The pooled sensitivity was 67% 95% [CI0.616–0.721], and the range was 22% [95% CI0.145–0.317] and 100% [95% CI0.735–1.000]. The sensitivity is low compared to the WHO and FDA standards and majority of the test kits that were used did not meet the approval of FDA and WHO
Balance of Benefits and Harms	Favors the use of RATs (N=1)	Probably favors the use of RATs (N=4)	Varies				RAT is more affordable, easy to use and with fast results
Certainty of Evidence	High	Moderate (N=2)	Low (N=2)	Very low (N=1)			There is downgrading because of the risk of inconsistencies and risk of bias The pooled specificity of RATs in this study was 100% [95% CI 0.997–1.000] however the pooled sensitivity was low at 67% 95% [CI0.616–0.721]
Accuracy	Very Accurate	Accurate (N=2)	Inaccurate (N=1)	Very Inaccurate	Varies (N=2)	Don't Know	

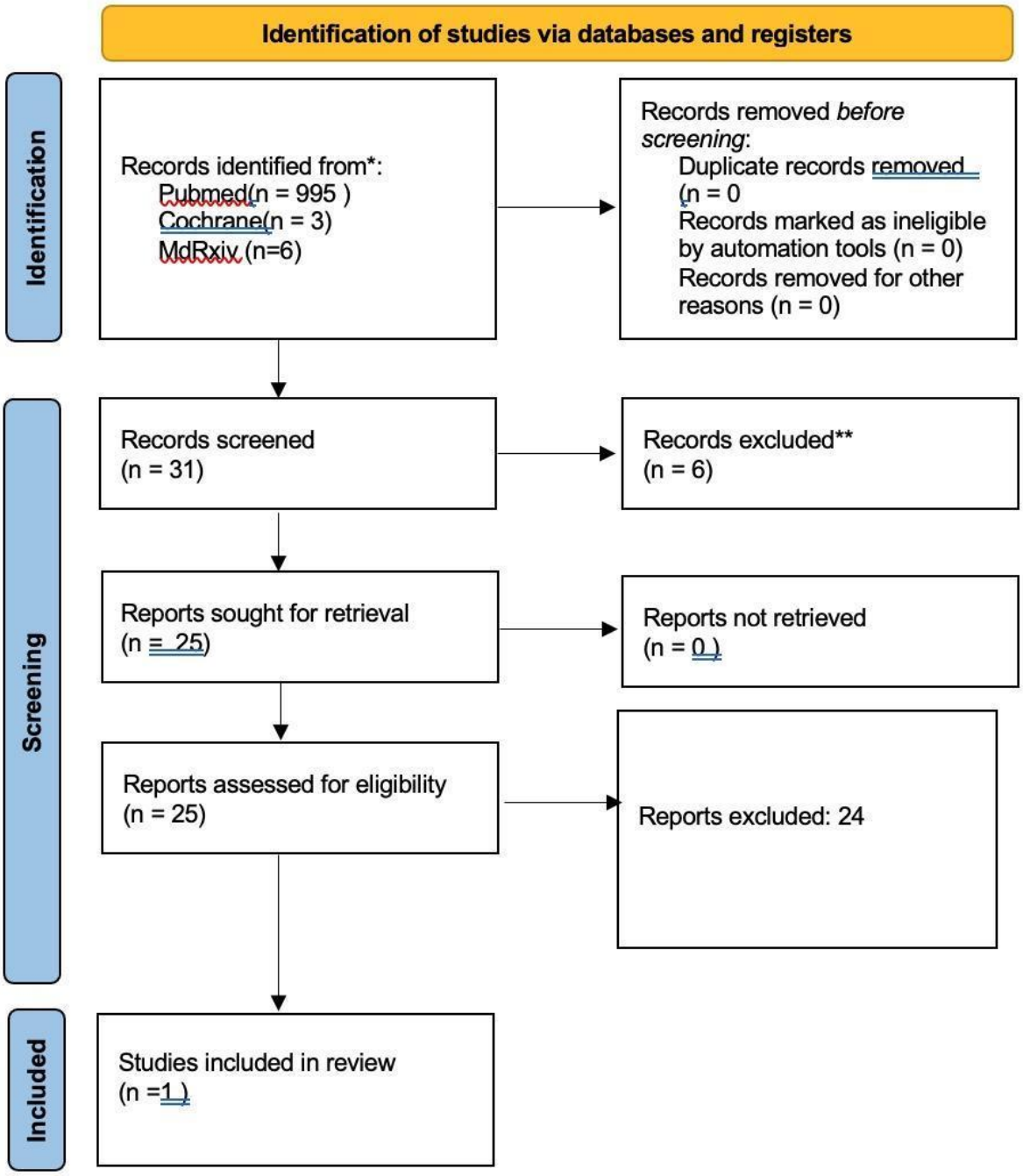
Values	Important uncertainty or variability	Possibly important uncertainty or variability (N=4)	Possibly NO important uncertainty or variability (N=1)	No important uncertainty or variability			None
Resources Required	Don't Know	Large cost	Moderate Cost (N=3)	Negligible cost	Moderate savings (N=1)	Varies (N=1)	Prices: The rapid antigen kit costs ₱350-700 COVID RT-PCR plate-based costs ₱1200-3400 for hospital-based and ₱900-5000 pesos for non-hospital based. As seen on the DOH website
Certainty of evidence of required resources	No included studies (N=2)	Very low	Low	Moderate (N=3)	High		
Cost effectiveness	No included studies (N=2)	Favors the comparator	Does not favor either RATs or the comparator	Probably favors RATs (N=3)	Favors criteria		
Equity	Reduced (N= 1)	Probably Reduced (N=1)	Probably no impact	Probably Increased (N=3)	Increased	Varies	
Acceptability	Don't Know	No	Probably No	Yes (N=2)	Probably yes (N=3)	Varies	Your consideration: lower cost for diagnosis of symptomatic patients

Feasibility	Don't Know	No	Probably No	Yes (N=5)	Probably yes	Varies	

Appendix 2: Search strategy

Database	Search strategy
PubMed	((omicron[Title/Abstract]) OR (COVID-19 Virus variants[Title/Abstract]) OR (SARS-CoV-2 BA.5 variant[Title/Abstract]) OR (SARS-CoV-2 B.1.1.529.2 variant[Title/Abstract]) OR (SARS-CoV-2 omicron subvariant BA.2[Title/Abstract]) OR (SARS-CoV-2 BA.2 variant[Title/Abstract]) OR (SARS-CoV-2 omicron variant[Title/Abstract]) OR (B.1.1.529 SARS-CoV-2 variant[Title/Abstract]) OR (COVID-19 Virus variant B.1.1.529[Title/Abstract]) OR (SARS-CoV-2 21K variant[Title/Abstract]) OR (SARS Coronavirus 2 variant B.1.1.529[Title/Abstract]) OR (omicron SARS-CoV-2 variant[Title/Abstract]) OR (SARS-CoV-2 B.1.1.529 variant[Title/Abstract]) OR (SARS-CoV-2 B.1.1.529[Title/Abstract]) OR (SARS-CoV-2 BA.1 variant[Title/Abstract])) AND ((rapid antigen test[Title/Abstract]) OR (rapid antigen detection[Title/Abstract]) OR (rapid antigen diagnosis[Title/Abstract]) OR (rapid antigen diagnostic[Title/Abstract]) OR (antigen rapid test[Title/Abstract]) OR (antigen rapid detection[Title/Abstract]) OR (antigen rapid diagnosis[Title/Abstract]) OR (antigen rapid diagnostic[Title/Abstract]) OR (antigen test[Title/Abstract]) OR (antigen detection[Title/Abstract]) OR (antigen diagnosis[Title/Abstract]) OR (antigen diagnostic[Title/Abstract]) (lateral flow[Title/Abstract]))
Cochrane	(((TITLE-ABS-KEY (omicron) OR TITLE-ABS-KEY (ba.5) OR TITLE-ABS-KEY (b.1.1.529.2) OR TITLE-ABS-KEY (ba.2) OR TITLE-ABS-KEY (ba.1) OR TITLE-ABS-KEY (ba.4) OR TITLE-ABS-KEY (ba.3))) AND (TITLE-ABS-KEY (rapid AND antigen AND test))) OR (((TITLE-ABS-KEY (rapid AND antigen AND test) OR TITLE-ABS-KEY (rapid AND antigen AND detection) OR TITLE-ABS-KEY (rapid AND antigen AND diagnosis) OR TITLE-ABS-KEY (rapid AND antigen AND diagnostic) OR TITLE-ABS-KEY (antigen AND rapid AND test) OR TITLE-ABS-KEY (antigen AND rapid AND detection) OR TITLE-ABS-KEY (antigen AND rapid AND diagnosis) OR TITLE-ABS-KEY (antigen AND rapid AND diagnostic) OR TITLE-ABS-KEY (antigen AND test) OR TITLE-ABS-KEY (antigen AND detection) OR TITLE-ABS-KEY (antigen AND diagnosis) OR TITLE-ABS-KEY (antigen AND diagnostic) OR TITLE-ABS-KEY (lateral AND flow)))
medrxiV	(TS=(b.1.1.529.2) OR TS=(omicron) OR TS=(BA.1) OR TS=(BA.2) OR TS=(BA.3) OR TS=(BA.4) OR TS=(BA.5)) AND (TS=(rapid antigen test) OR TS=(rapid antigen detection) OR TS=(rapid antigen diagnosis) OR TS=(rapid antigen diagnostic) OR TS=(antigen rapid test) OR TS=(antigen rapid detection) OR TS=(antigen rapid diagnosis) OR TS=(antigen rapid diagnostic) OR TS=(antigen test) OR TS=(antigen detection) OR TS=(antigen diagnosis) OR TS=(lateral flow))

Appendix 3: PRISMA Flow Diagram of Literature Search



Appendix 4: GRADE Evidence Profile

Question: Should Rapid Antigen Test be used to diagnose Omicron Variant in among patients with Covid 19 Infection?

Sensitivity	0.67 (95% CI: 0.59-0.72)
Specificity	1.00 (95% CI: 1.00-1.00)

Prevalences	2%	5%	10%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE	Importance
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	pre-test probability of5%	pre-test probability of10%		
True positives (patients with Omicron Variant)	1 studies 0 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	very serious[b]	not serious	none	13 (12 to 14)	34 (30 to 36)	67 (60 to 72)	⨁◯◯◯ Very low	CRITICAL
False negatives (patients incorrectly classified as not having Omicron Variant)								7 (6 to 8)	16 (14 to 20)	33 (28 to 40)		CRITICAL
True negatives (patients without Omicron Variant)	1 studies 0 patients	cross-sectional (cohort type accuracy study)	serious	not serious	very serious[b]	not serious	none	980 (977 to 980)	950 (947 to 950)	900 (897 to 900)	⨁◯◯◯ Very low	CRITICAL
False positives (patients incorrectly classified as having Omicron Variant)								0 (0 to 3)	0 (0 to 3)	0 (0 to 3)		CRITICAL
Inconclusive	0 studies 0 patients	-	-	-	-	-	-				-	
Complications	0 studies patients										-	

Explanations

a. D. Were the index test results interpreted without knowledge of the results of the reference standard?
b. There was high heterogeneity among the studies, as evidenced by the i2=

Appendix 5: Appraisal (AMSTAR and Painless EBM)

AMSTAR Checklist

Printer Friendly Version

Article Name: Clinical Performance of Rapid Antigen in Comparison to RT-PCR for SARS-COV2 in Diagnosis in Omicron Variant: A Systematic Review and Meta-analysis.

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:	Optional (recommended)	
Y Population	☐ Timeframe for follow up	Y Yes
Y Intervention		☐ No
Y Comparator group		
Y Outcome		

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and di the report justify any significant deviations from the protocol?

For Partial Yes: The authors state that they had a written protocol or guide that included ALL the following:	For Yes: As for partial yes, plus the protocol should be registered and should also have specified:	
Y review question(s)	Y a meta-analysis/synthesis plan, if appropriate, and	Y Yes
Y a search strategy	Y a plan for investigating causes of heterogeneity	☐ Partial Yes
Y inclusion/exclusion criteria	Y a plan for investigating causes of heterogeneity	☐ No
Y a risk of bias assessment		

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:

☐ Explanation for including only RCTs	Y Yes
☐ OR Explanation for including only NRSI	☐ No
OR Explanation for including both RCTs and NRSI	

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):	For Yes, should also have (all the following):	
Y searched at least 2 databases (relevant to research question)	Y searched the reference lists / bibliographies of included studies	☐ Yes
Y provided key word and/or search strategy	☐ searched trial/study registries	Y Partial Yes
	☐ included/consulted content experts in the field	☐ No
	☐ where relevant, searched for grey literature	
	Y conducted search within 24 months of completion of the review	

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:

Y at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include

☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.

Y Yes
☐ No

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following:

☐ at least two reviewers achieved consensus on which data to extract from included studies

☐ OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.

☐ Yes
Y No

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes:	For Yes, must also have:	
Y provided a list of all potentially relevant studies that were read in full-text form but excluded from the review	Y Justified the exclusion from the review of each potentially relevant study	Y Yes ☐ Partial Yes ☐ No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following):	For Yes, should also have ALL the following:	
Y described populations	Y described population in detail	Y Yes
Y described interventions	Y described intervention in detail (including doses where relevant)	☐ Partial Yes ☐ No
Y described comparators	Y described comparator in detail (including doses where relevant)	
Y described outcomes	Y described study's setting	
Y described research designs	Y timeframe for follow-up	

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs

For Partial Yes, must have assessed RoB from	For Yes, must also have assessed RoB from:	
☐ unconcealed allocation, and	☐ allocation sequence that was not truly random, and	☐ Yes Y Partial Yes ☐ No ☐ Includes only NRSI

NRSI

For Partial Yes, must have assessed RoB:	For Yes, must also have assessed RoB:	
Y from confounding, and	☐ methods used to ascertain exposures and outcomes, and	☐ Yes Y Partial Yes
Y from selection bias	Y selection of the reported result from among multiple measurements or analyses of a specified outcome	☐ No ☐ Includes only RCTs

10. Did the review authors report on the sources of funding for the studies included in the review?

For Yes

☐ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies	☐ Yes Y No

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

RCTs

For Yes:

Y The authors justified combining the data in a meta-analysis

Y AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present.

Y AND investigated the causes of any heterogeneity

Y Yes
☐ No
☐ No meta-analysis conducted

For NRSI

For Yes:

Y The authors justified combining the data in a meta-analysis

Y AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present

Y AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available

☐ AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review

Y Yes
☐ No
☐ No meta-analysis conducted

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes:

☐ included only low risk of bias RCTs

Y OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.

Y Yes
☐ No
☐ No meta-analysis conducted

13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?

For Yes:

☐ included only low risk of bias RCTs

Y OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results

Y Yes
☐ No

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes:

☐ There was no significant heterogeneity in the results	Y Yes ☐ No
Y OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review	

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes:

Y performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	Y Yes ☐ No ☐ No meta-analysis conducted

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

For Yes:

Y The authors reported no competing interests OR	Y Yes ☐ No
☐ The authors described their funding sources and how they managed potential conflicts of interest	

To cite this tool: Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

Legend: Those with Y means that it is yes or present in the article

APPRAISAL FORM FOR A SYSTEMATIC REVIEW OR META-ANALYSIS

"Clinical performance of rapid antigen tests in comparison to RT-PCR for SARS-COV-2 diagnosis in Omicron variant: A systematic review and meta-analysis"

Zahra Eslami Mohammadie et al

RESEARCH QUESTION: Among patients suspected to have COVID-19, how accurate are rapid antigen tests compared to RT-PCR for the diagnosis and screening of COVID-19 for the Omicron variant?

Christine S. Caringal, MD and Joan Roque-Viado, MD

<table>
<tr><td>I. APPRAISING DIRECTNESS</td><td></td></tr>
<tr><td>Does the study provide a direct enough answer to your clinical question in terms of type of patients (P), exposure/ intervention (E) and outcome (O)?</td><td>
<table>
<tr><td></td><td>scenario</td><td>article</td></tr>
<tr><td>P</td><td>patients suspected to have COVID-19</td><td>patients suspected to have COVID-19</td></tr>
<tr><td>E</td><td>RAT</td><td>RAT</td></tr>
<tr><td>C</td><td>RT – PCR</td><td>RT - PCR</td></tr>
<tr><td>O</td><td>Covid 19</td><td>Covid 19</td></tr>
</table>
</td></tr>
<tr><td>II. APPRAISING VALIDITY</td><td></td></tr>
<tr><td>Were the criteria for inclusion of studies appropriate?</td><td>YES
INCLUSION
- English language journal articles that assessed the clinical performance of RATs for SARS-COV-2 diagnosis compared with RT-PCR as the reference standard in patients infected with the Omicron as the last variant of concern (VOC)
- Reports that used a valid method for viral genotyping in order to ensure the kit's performance in the Omicron variant
- Studies which used adequate numbers (at least 5 confirmed Omicron samples) of clinical specimens obtained from COVID-19-suspected humans, not standard samples, recombinant proteins, etc.
-Published original articles on diagnostic, cohort and cross-sectional studies
EXCLUSION
- unrelated papers, reviews and editorial articles and case reports</td></tr>
</table>

	- Preprint articles and non-English full texts
2. Was the search for eligible studies thorough?	NO Did not utilized pre prints , only English language journal articles only Search strategy: We performed a systematic search in PubMed, Scopus, Web of Science and Embase databases on 01 August 2022. The search terms included “Omicron”, “B.1.1.529”, “rapid antigen test”, and “lateral flow test”. The detailed search strategy is shown in the supplementary material (Table S1). We used no additional filter. Furthermore, we performed a hand search of the reference lists of related articles from the primary search; also, we checked the first 25 pages of Google Scholar after a simple search on the topic for completeness. Since many new studies on this hot topic were published day by day, we updated the search in the above-mentioned databases on 26 August 2022.
Was the validity of the included studies assessed?	YES Two people independently appraised the quality of the included articles using the **JBI checklist for diagnostic test accuracy quality assessment.** A total of four individuals were employed for resolving the contradictions of quality assessment. Finally, we excluded the studies with unacceptable quality.
Were the assessments of the studies reproducible?	Two people independently appraised the quality of the included articles A total of four individuals were employed for resolving the contradictions of quality assessment. Finally, we excluded the studies with unacceptable quality.
III. APPRAISING RESULTS	
1. What are the overall results of the review?	The outcomes of the study were presented in 2 forest plots **F I G U R E 3** Forest plot for studies reporting sensitivity. **F I G U R E 4** Forest plot for studies reporting specificity.
2. How precise were the results?	Yes, Specificity: YES : because the CI of the diamond is narrower than the individual studies. it is in favors the intervention.

	It does not cross 1 Sensitivity: crosses the line of 1, then there is no significant difference between using and not using the test
3. Were the results similar from study to study?	There is substantial heterogeneity Sensitivity: heterogeneity: I^2=88% χ^2= 0.6986 p < 0.01 Specificity: heterogeneity: I^2=84% χ^2= 10.3602 p <0.01 All subgroup analyses had high levels of heterogeneity **except** for symptomatic group analyses ($I2$ = 39%)
IV. ASSESSING APPLICABILITY	
Are there biologic issues affecting applicability? (Consider the influence of sex, co-morbidity, race, age and pathology)	Sex: none Co-morbidity: none Race: none Age: none Pathology: yes (Viral Load)
Are there socio-economic issues affecting applicability?	None RAT is cheaper and easier to do
If the overall results of the review are not directly applicable to your patient, are there credible subgroup analyses that you could use?	Overall results are applicable to our population
V. INDIVIDUALIZING THE RESULTS	
What is the implication of study findings on your individual patient? (Estimate the individualized NNTs for your patient)	Post Test Probability: 70.9 % for RAT for omicron Lower than the recommendation of the WHO which 80%
2. Would you offer the treatment to your patients?	

COMPUTATION

A 1268	B 5382
C 2551	D 4406

$$LR(+) = \frac{(a/b)}{(a+c\ /\ b+d)} = \frac{1268/\ 5382}{3819/9788} = \frac{0.236}{0.39} = 0.61$$

Step 1. Pretest probability : 80 %

Step 2: Convert pre-test probability to odds : $\frac{80}{100-80} = \frac{80}{20} = 4\%$

Step 3: Multiply pre-test odds by the LR of the test. result to get the post-test odds = 4 x 0.61 = 2.44%

Step 4: Convert post-test. odds back to post-test. probability in per cent $\frac{2.44}{1 + 2.44} \times 100 = 70.9\%$

Appendix 6: Studies included in the Systematic Review and Meta analysis of Mohammadie et al.

First author	Country	Sampling date	Study Design	Number of participants
1Garcia-Cardenas, et al	Mexico	15 Dec 2021 to 5 Jan 2022	cohort	783
2 Sabrina Jungnick, et al	Germany	13 Dec 2021 to 24 Dec 2021	cohort	51
3 John Schrom et al	USA	3 Jan 2022 to 4 Jan 2022	cohort	731
4 Jean Lous Bayart, et al	Belgium	1 Jan 2022 to 6	cohort	120
5. Anuradha, Rao et al	USA	no mention	cohort	29
6. Alessandro Medoro, et al	Italy	Dec 2021 and Feb 2022	cohort	584
7. Lihong Liu, et al	USA	No mention	cohort	1148
8. Justin Hardick et al	USA	22 Nov 2021 and 31 Dec 2021	cohort	14
9. Andreas Osterman et al	Germany	26 Nov 2021 and 1 Jan 2022	cohort	115
10. Maria A. Kyristi et al	Greece	No mention	cohort	219
11. Aurelie Gourgeon et al	France	Jan 2022	cohort	
12. Gert Marais, et al	South Africa	19 Nov 2021 and 8 Dec 2021	cross sectional	453
13. Barbara L. Goodall et al	Canada	Jan 2022	cross-sectional	1,472
14. Meriem	Switzerland	No mention	cohort	113

Bekliz et al				
15. Karoline Leuzinger et al	Switzerland	25 Jan 2022-28Feb 2922 and 8 March 2022-15Jul 2022	cohort	150
16. Cinzia Peronace et al	Italy	No mention	cross-sectional	603
17. Jidapa Szekely et al	Thailand	August 2021 to September 2021	cross-sectional	319
18. Rafael Mello Galliez et al	Brazil	17 January 2022 to 7 February 2022	cohort	192

Appendix 7: Rapid Antigen Test Kits that were Used in the Study

WHO Approved	FDA Approved	NOT APPROVED	AVAILABLE IN THE PHILIPPINES
1. Panbio COVID-19 Ag RAPID N.M. Yes TEST DEVICE (NASAL), Abbott, Jena, German	CLINITEST rapid COVID-19 N.M. antigen Self-Test, Siemens Healthineers, Erlangen, Germany	COVISTIXTM rapid antigen test (Sorrento therapeutics, San Diego, CA, USA)	Panbio COVID-19 Ag RAPID N.M. Yes TEST DEVICE (NASAL), Abbott, Jena, German
2. Flowflex COVID-19 antigen N Home test (Acon Laboratories, San Diego, CA, USA)	Rapid SARS-CoV-2 antigen N.M. test Card, Xiamen Boson Biotech Co., Xiamen, China	ARS-CoV-2 rapid antigen test (self-test), Roche, Mannheim, Germany	Sofia SARS antigen FIA Quidel Sofia
3. Standard Q COVID-19 Ag (SD Biosensor/Roche	BinaxNOW rapid antigen test (Abbott)	NADAL COVID-19 Ag test Nal von Minden, Moers, Germany	NADAL COVID-19 Ag test Nal von Minden, Moers, Germany
4. Onsite COVID19 Ag rapid test (CTK Biotech)	Boson rapid SARS-CoV-2 N antigen test Card (Xiamen Boson Biotech Co., Xiamen, China)	BIOCREDIT COVID-19 Ag one step rapid test, Rapigen Inc., Anyang-si, South Korea	Sejoy SARS-CoV-2 antigen rapid test Cassette (Hangzhou Sejoy Electronics & Instrument Co., Hangzhou, China)
5. Sure status (Premier Medical Corporation	Flowflex COVID-19 antigen N Home test (Acon Laboratories, San Diego, CA, USA)	New-gene COVID-19 antigen detection kit (new-gene Bioengineering Hangzhou, China	Roche SARS-CoV-2 rapid antigen test nasal (Roche diagnostics, Basel, Switzerland
6.	Abbott molecular BinaxNow assay	Sejoy SARS-CoV-2 antigen rapid test Cassette (Hangzhou Sejoy Electronics & Instrument Co., Hangzhou, China)	Roche-SARS-CoV-2-antigen
7	Orasure InteliSwab assay	Roche SARS-CoV-2 rapid antigen test nasal (Roche diagnostics, Basel, Switzerland	Flowflex COVID-19 antigen N Home test (Acon Laboratories, San Diego, CA, USA)

8	**Quidel Quickvue assay**	**Wantai SARS-CoV-2 Ag rapid test, Eurobio Scientific, Wantai**	
9	**GenBody COVID-19 Ag**	**AMAZING COVID-19 antigen Sealing Tube test Strip (Colloidal gold) CoV-SCAN (BioMedomics, Inc.) (newly developed test)**	
10	**Sofia SARS antigen FIA Quidel Sofia**	**Becton Dickinson Veritor assay**	
11	**Test antigénique rapide Clinitest COVID-19 S healthcare Siemens**	**FUJIFILM COVID-19 Ag test (Fujiflm Cooperation)**	
12		**Novel Coronavirus 2019 nCoV antigen test (Colloidal gold) (Beijing Hotgen Biotech Co., Ltd.)**	
13		**NanoRepro SARS-CoV-2 antigen Schnelltest (Viromed) (NanoRepro AG)**	
14		**Lyher novel Coronavirus (COVID-19) antigen test kit (Colloidal gold) (Hangzhou Laihe Biotech Co., Ltd.)**	
15		**COVID-19 Ag BSS self-test (Biosynex Swiss SA)**	
16		**Rapid SARS-CoV-2 antigen test Card (MP Biomedicals Germany GmbH)**	

17		**MedicovidAG SARS-CoV-2 antigen rapid test Card-nasal (Xiamen Boson Biotech Co., Ltd.)**	
18		**Rapid test Ag 2019-nCov (PROGNOSIS, BIOTECH, Larissa, Greece)**	
19		**COVID-VIRO antigen rapid test, AAZ, AAZ**	
20		**CerTest SARS-CoV-2 card test, CerTest Biotec, CerTest**	
21		**Nadal COVID-19 Ag test, Nal von Minden, Nadal**	
22		**Rapid test antigen GenSure COVID-19, GenSurem, GenSure**	
23		**AMP rapid test SARS-CoV-2 Ag, AMP diagnostics, AMP**	
24		**QuickProfile COVID-19 antigen test, LumiQuick Diagnostics, QuickProfile**	
25		**Novel coronavirus (COVID-19) antigen test kit, Medakit, novel**	
26		**Toda Coronadiag Ag, Toda Pharma, Toda Pharma**	
27		**Wantai SARS-CoV-2 Ag rapid test, Eurobio Scientific, Wantai**	
28		**ARS-CoV-2 antigen rapid detection kit Genomic Vision Genomic Vision**	

29		**RealityTech antigen test COVID 19 Fasual Care Fasual Care**	
30		**COVID-19 antigen rapid test . Servibio Servibi**	
31		**Humasis one-step COVID-19 Ag test Eurobio Scientific Humasis**	
32		**BSD-0500333-25- COVID19 speed antigen test Biospeedia Biospeedia**	
33		**SARS-CoV-2 spike colloidal S gold chromatographic assay R-Biopharm R-Biopharm**	
34		**NG-test COVID19 NG-Biotech NG Biotech 2**	
35		**Indicaid COVID-19 rapid antigen test Medisur Medisur**	
36		**PCL test COVID Ag Tanit Care Tanit Care**	
37		**Biosensor standard F COVID-19 Ag FIA Orgentec Orgentec**	
38		**Rapid Response Ag-RDT N.M. (BTNX)**	
39		**2019- nCoV antigen test (Wondfo)**	
40		**Beijng Tigsun diagnostics Co. Ltd. (Tigsun)**	
41		**Roche-SARS-CoV-2-antigen**	

42		**GeneFinder COVID-19 Ag plus rapid test**	
43		**KestrelTM COVID-19 Ag rapid test)**	