Use of COVID-19 IgG and IgM Rapid Diagnostic Test (RDT) Kits for Mild and Asymptomatic At-Risk COVID-19 Cases

RAPID REVIEW

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1. CONTEXT AND POLICY ISSUES

In early 2020, the World Health Organization (WHO) declared severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing novel coronavirus disease 2019 (COVID-19) as a global pandemic affecting more than 160 countries and regions with at least 350,000 cases and 15,000 deaths worldwide as of 23 March 2020 (Dong, Du & Gardner, 2020). In the Philippines, COVID-19 affected over 400 cases with 33 deaths as of 23 March 2020 (DOH, 2020). Local mortality rate of 7.14% is slightly higher compared to the global mortality rate (3%-6%). Note that the rates do not fully account for the asymptomatic cases. To date, treatment remains unknown. (Dong, Du & Gardner, 2020; DOH, 2020)

In response to this public health emergency, the Philippine Department of Health has implemented a triage algorithm in conducting diagnostic testing for patients with suspected cases of COVID-19. The algorithm referred to patients presenting acute respiratory illness who may be classified as persons under monitoring or persons under investigation, depending on the history of exposure, travel history and pre-existing conditions. Currently, the algorithm does not recommend testing for those presenting mild symptoms (and with travel history to any country or area with local transmission of COVID-19 or with close contact to a confirmed COVID-19 case, however, no symptoms occurred within the past 14 days of observation) and those considered asymptomatic at-risk. (DOH, 2020)

Currently, real time reverse transcriptase polymerase chain reaction (RT-PCR) is the standard diagnostic method for diagnosis of COVID-19. However, some limitations such as long turnaround time of two to three hours and strict requirements on the facilities and manpower to perform the tests, make it less ideal for use in the field for rapid screening of patients suspected of COVID-19. These limitations resulted in a need for use of other methods to diagnose patients suspected of COVID-19 for a shorter period such as COVID-19 IgG and IgM Rapid Diagnostic Test (RDT) Kits, a rapid point-of-care lateral flow immunoassay for the detection of IgG and IgM antibodies against SARS-CoV-2 virus in human blood (Li et al, 2020). As of writing, there is no conclusive guidance on the use of COVID-19 IgG and IgM Rapid Diagnostic Test Kits for mild and asymptomatic at-risk COVID-19 cases. Although the sensitivity and specificity of immunoassay may be high, these may still vary depending on key factors such as patient age, microbial serotype, specimen type, or stage of clinical diseases (Andreotti et al, 2018). Amid public clamor for mass testing for Filipinos including those who are either asymptomatic or with mild symptoms, even without history of exposure, evidence is needed to support this proposition.

As such, **a rapid review was conducted to search for and synthesize existing COVID testing guidelines from selected healthcare systems** for asymptomatic or with mild symptoms at-risk COVID-19 cases, as well as existing **evidence on the clinical accuracy, and cost-effectiveness of the use of COVID-19 IgG and IgM RDT Kits for mild and asymptomatic at-risk COVID-19 cases.**

2. POLICY AND RESEARCH QUESTIONS

POLICY QUESTION

Should the Philippine government introduce COVID-19 IgG and IgM RDT kits in detecting COVID19 cases among mild and asymptomatic at-risk cases *versus no testing?*

RESEARCH QUESTIONS

1. **What are the evidence-based guidelines for the use of COVID-19 IgG and IgM RDT kits among mild and asymptomatic at-risk cases? What are the current COVID-19 testing protocols among healthcare systems?**

2. **What is the accuracy of COVID-19 IgG and IgM RDT kits in detecting COVID19 cases among mild and asymptomatic at-risk cases *versus gold standard testing?***

3. **Does COVID-19 IgG and IgM RDT kits represent value for money (in terms of cost per additional case detected) in detecting COVID19 among mild and asymptomatic at-risk cases *versus no testing?***

3. KEY FINDINGS

The current WHO Interim Guidance does not currently recommend rapid disposable tests for antigen/ antibody detection for COVID-19 in the context of clinical diagnosis. More evidence is needed on test performance and operational utility. Among existing COVID-19 testing guidelines across different countries detected and reviewed, only one country (i.e, South Korea) shows to offer diagnostic testing for mild and asymptomatic at-risk cases, but using RT-PCR. Singapore allows testing of healthcare personnel with mild symptoms.

As with existing clinical evidence on the accuracy of COVID-19 IgG and IgM RDT kit, we found only one study which fulfilled our selection criteria and was included in our rapid review. According to this study by Li et al, 2020 conducted in China, COVID-19 IgG and IgM RDT kit has a specificity of 90.63% and sensitivity of 88.66%. However, our appraisal of this study shows the gold standard used was not specified. It was also not specified if the performance and interpretation of the gold standard and the index tests were independent. Furthermore, the study made use of known positives and known negatives in the evaluation of the test creating an artificial prevalence of 75% which is much higher compared to the Philippine population. The detection limit for this RDT kit has not been determined yet. As no strong evidence on the real accuracy of immunoassay for COVID-19 is established yet, the likelihood of false negative from immunoassays in general should be considered.

In terms of its cost-effectiveness, no existing evidence was identified. Note however that in general, mass testing is considered to be costly and can be challenging for a variety of reasons including access, adherence, awareness, and training.

As evidence on the different facets of COVID-19 is on-going and rapidly evolving, regular scoping for evidence and updating of recommendations are advised.

4. METHODS

4.1 Literature Search Methods

Two reviewers for the clinical efficacy studies and three reviewers for the protocols/ guidelines and economic evaluations performed a limited literature search for relevant studies published from inception to 23 March 2020 via PubMed for the clinical efficacy studies; and, via PubMed LitCovid and websites of major international HTA agencies (ie, UK National Institute for Health and Care Excellence, Canadian Agency for Drugs and Technologies in Health, Africa, Australia, Germany, Swedish Agency for Health Technology Assessment) for the cost-effectiveness studies. The current guidelines and testing protocols of selected countries were searched through individual country websites as provided and linked by *UptoDate®*. Search terms used were rapid diagnostic test, lateral flow immunoassay, and MESH terms for nCov-19 and point of care testing. No filters/restriction on study type, language and publication date were applied.

4.2 Selection Criteria and Methods

Two reviewers for the clinical efficacy studies and three reviewers for the protocols/guidelines and economic evaluations screened the total citations and selected the studies with supervision. The full text of potentially eligible studies with relevant abstracts and titles were retrieved and evaluated for eligibility using the set inclusion and exclusion criteria.

Table 1: Inclusion Criteria	
Population	Mild and asymptomatic at-risk COVID-19 patients *Mild at-risk COVID-19 cases* - patients with history of exposure and have no comorbidities, non-elderly, and show only mild clinical symptoms (ie, fever, dry cough, fatigue, sputum production, sore throat, headache, myalgia or arthralgia, chills, nausea and vomiting, nasal congestion, diarrhea) *Asymptomatic at-risk COVID-19 cases* - patients with history of exposure and have no comorbidities, non-elderly, and shows no clinical symptoms (ie, fever, dry cough, fatigue, sputum production, sore throat, headache, myalgia or arthralgia, chills, nausea and vomiting, nasal congestion, diarrhea, difficulty of breathing)
Intervention / Exposure	COVID-19 IgG and IgM RDT kits
Comparator	Clinical accuracy: RT-PCR Cost-Effectiveness: No testing
Outcomes	Clinical efficacy/ effectiveness: Sensitivity, Specificity Cost-effectiveness: cost case detected *(such as but not limited to the outcome measures listed above)*

Study Designs	Health technology assessments, systematic reviews (SRs), meta-analyses, primary diagnostic accuracy studies, economic evaluations, guidelines and protocols

Exclusion Criteria
Articles were excluded if they did not meet the selection criteria outlined in Table 1 or they were duplicate publications.

4.3 Critical Appraisal of included studies

Two reviewers for the clinical efficacy studies and three reviewers for the protocols/ guidelines and economic evaluations extracted and summarized the key data domains using a standard data extraction tool. The following appraisal tools were then applied to evaluate the quality of the included clinical and cost-effectiveness studies:

- Primary diagnostic accuracy studies: *Evaluation of Articles on Diagnosis (Dans et al, 2017)*
- Economic evaluations: *Drummond et al, 1996 tool*

5. SUMMARY OF EVIDENCE

5.1 COVID-19 Testing Guidelines and Protocols

According to the WHO Interim Guidance published on March 22, 2020 titled, *Laboratory testing strategy recommendations for COVID-19,* "Serological assays will play an important role in research and surveillance but are not currently recommended for case detection and are not included in this document. The role of rapid disposable tests for antigen detection for COVID-19 needs to be evaluated and is not currently recommended for clinical diagnosis pending more evidence on test performance and operational utility. "

An exhaustive *UptoDate®* search of the various guidelines of the countries revealed that only South Korea allows for testing of mild and asymptomatic at-risk cases but using RT-PCR, while the other countries/ territories like Canada, USA, United Kingdom, Europe, Australia and China recommend self-quarantine for those with mild and asymptomatic cases. Some countries offer free testing for mild and asymptomatic cases; however, those are only under special cases and for patients with higher risk. Singapore offers free testing for mild cases for health workers and known contacts of COVID-19 positive patients, while Thailand offers free testing for mild cases for patients with recent travel history to crowded places.

Currently, RDT kits for Covid-19 IgG and IgM are only registered at the European Union under a CE-IVD registration. Based on our search, no country has included these kits as a nationwide testing strategy.

Appendix 1 shows a summary of the different COVID-19 testing protocols/ guidelines per country.

5.2 Clinical Efficacy or Accuracy of COVID-19 IgG and IgM RDT kits

5.2.1 Quantity of Research Available and General Study Characteristics

The reviewers identified a total of 17 citations in the literature search, all from medical databases as no relevant citations were identified from major international health technology agencies. Of these total citations, 14 titles and abstracts that did not meet the inclusion criteria were excluded leaving 3 potentially relevant citations. Of these potentially relevant full text articles, one (Li et al, 2020) was included in the review. Appendix 1 illustrates the PRISMA flowchart of the study selection.

The included study assessed the clinical/diagnostic accuracy of the developed IgG and IgM RDT kit. Patients who were recruited had to conform with the diagnostic criteria of a suspected case of COVID-19 according to guidelines of diagnosis and treatment of COVID-19 of the China Center for Disease Control. The RDT was not compared with any existing diagnostic test used for detecting COVID-19. Study characteristics of included publications are tabulated in Appendix 2.

5.2.1 Summary of Critical Appraisal (Li et al, 2020)

XueFeng Wang ORCID iD: 0000-0001-8854-275X
Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis

I. APPRAISING DIRECTNESS	
Does the study provide a direct enough answer to your clinical question in terms of patients (P), examination (E) used and disease or outcome (O) being diagnosed?	No. The study was done among known and unknown cases of COVID-19. In our setting, the question is whether it can be used among asymptomatic or those with mild symptoms.
II. APPRASING VALIDITY	
1. Was the reference standard an acceptable one?	No mention on what was used as the reference standard. On page 6, it is stated *"The respiratory tract specimen, including pharyngeal swab and sputum, was used to confirm COVID-19 cases"* but it was not mentioned what laboratory technique was used to confirm the COVID-19.
2. Was "definition" of the index test and the reference standard independent?	No definition of index test is provided.
3. Was "performance" of the index test and the reference standard independent?	It was not mentioned if the performance of the test and reference standard are independent. It is likely not to be since they selected specimens of known and unknown COVID-19 which suggests that the supposed gold standard was already known when they selected the patients for inclusion. Regardless of the test results, the

	investigators performed the test and the gold standard independently.
4. Was "interpretation" of the index test and the reference standard independent?	It was not mentioned if the interpretation of the index test and reference standards are independent. However, it is likely not to be independent since the results of the supposed gold standard was already known when the participants were included in the study.
III. APPRAISING RESULTS	
What were the likelihood ratios of the various test results?	**Characteristic** / **Results** / **95% CI** Sensitivity / 88.66% / 85.13% to 91.61% Specificity / 90.62% / 84.20% to 95.06% PPV / 96.70% / 94.47% to 98.05% NPV / 72.05% / 66.07% to 77.34% LR (+) / 9.46 / 5.51 to 16.23 LR (-) / 0.13 / 0.09 to 0.17
IV. ASSESSING APPLICABILITY	
1. Are there biologic issues that may affect accuracy of the test? (Consider the influence of sex, co-morbidity, race, age and pathology)	None identified
2. Are there socio-economic issues that may affect accuracy of the test?	The cost of the test should be considered
V. INDIVIDUALIZING THE RESULTS	
1. How will the test results affect the probability of disease in your patient? (Estimate the individualized post-test probability of your patient)	N/A
2. Is this test useful for your patient?	N/A

5.2.3 Summary of Findings

Based on the results of Li et. al., 2020 (see Appendix 3), 352 clinically confirmed positive patients tested positive using the RDT kit yielding a sensitivity of 88.86%, while 12 clinically confirmed negative samples tested positive on the RDT test yielding a specificity of 90.63%.

The study has identified several reasons for having false negatives. First, they identified that when antibody concentration (i.e., IgG and IgM) levels are below the detection limit of this rapid test, the test results will be negative. However, the detection limit for this test has not been determined yet. Second, people have varying responses in producing these antibodies. Lastly, it was noted that IgM decreases and disappears after 2 weeks; thus, its level is below its peak and not detectable by the test.

According to the study authors, potential applications of the developed IgG-IgM combined antibody test kit includes rapid field detection and screening for asymptomatic SARS-CoV-2 carriers. However, while the test saves time and does not require equipment, it cannot confirm the presence of the virus, rather only evidence of recent infection. Furthermore, cross-reactivity with other coronaviruses and flu viruses were not studied.

5.3 Cost-effectiveness of COVID-19 IgG and IgM RDT kits

There was no relevant evidence regarding the cost-effectiveness of COVID-19 IgG and IgM RDT kits, to date; therefore, no summary to support its cost-effectiveness or efficiency can be provided. It has to be noted, however, that testing for pre-symptomatic persons, in general, is costly and difficult to implement in consideration to access, adherence, awareness, and training. Appendix 4 shows the systematic search performed for this section.

6. LIMITATIONS

This review recognizes the following limitations: First, as this is a rapid review, certain steps of a systematic review were abbreviated. Second, as very limited evidence measuring the clinical accuracy of the test was identified, the findings and conclusion of this review in terms of its clinical accuracy was based only on one existing study, to date. Third, as evidence on the different facets of COVID-19 is on-going and rapidly evolving, the evidence presented here can rapidly change as well.

7. CONCLUSION

The WHO Interim Guidance (March 22, 2020) considers serological assays to play an important role in research and surveillance but are not currently recommended for case detection. The guidance does not currently recommend rapid disposable tests for antigen and/or antibody detection for COVID-19 for clinical diagnosis, pending more evidence on test performance and operational utility. Testing policy guidance across different countries generally show testing for severe symptomatic cases using RT-PCR,

while mild and asymptomatic cases are generally advised for self-quarantine at home. In the Philippines, current COVID-19 guidelines only refer to government-covered testing of patients presenting severe symptoms of suspected COVID-19 or mild and asymptomatic at-risk patients who are elderly, or with comorbidity. Meanwhile, in South Korea testing is available even for asymptomatic or mildly symptomatic at-risk patients. It is also important to note that RT-PCR was used for testing of all countries seen in this review. There are currently no local and international FDA registrations for COVID-19 IgG and IgM RDT kits, except for CE-IVD registration for the European Union.

There was only one accuracy study found in this review (Li et al, 2020) shows that COVID-19 IgG and IgM RDT has a specificity of 90.63% and sensitivity of 88.66%. However, based on our appraisal of this study, we found there were considerable flaws in the study design. A fundamental flaw is the non-specified gold standard. Even so, there was no mention of the independence of the performance and interpretation of the index test and the gold standard. It is not surprising that the positive predictive value of the test is very high because the (artificial) prevalence of COVID-19 in this study is greater than 75%. The findings of the appraisal make the results of the study questionable. Aside from the validity, the applicability is likewise questionable as the intent is to evaluate whether this test can be applied to those with mild disease or no disease which is unlike the population included in the study (see Table 1).

As no strong evidence on the real accuracy of immunoassay for COVID-19 is established yet, the likelihood of false negative from immunoassays in general should be considered. Furthermore, analytical specificity and sensitivity has not yet been determined as stated by the authors. Hence, cross reactivity with other coronaviruses and flu viruses as well as the detection limit has not yet been determined. In addition, while the study authors suggest that a potential application of the test kit is testing of asymptomatic patients, study results do not provide any evidence on clinical characteristics of the sampled patients, thus being unable to identify its accuracy with regards to screening of asymptomatic/mild cases.

There had been no economic evaluation studies to cost or show the efficiency of implementing COVID-19 IgG and IgM RDT for mild and asymptomatic cases. In general, however, it is noted that mass testing is considered to be costly and challenging for a variety of reasons including access, adherence, awareness, training and cost.

Finally, as evidence on the different facets of COVID-19 is on-going and rapidly evolving, regular scoping for evidence and updating of recommendations are strongly advised.

8. DECLARATION OF CONFLICT OF INTERESTS

The reviewers have no relevant affiliations or financial involvement with any organization or entity with a financial interest or in financial conflict with the subject matter or materials discussed in the review report.

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APPENDIX

Appendix 1. Protocols/ Guidance on COVID-19 testing among different countries/ settings

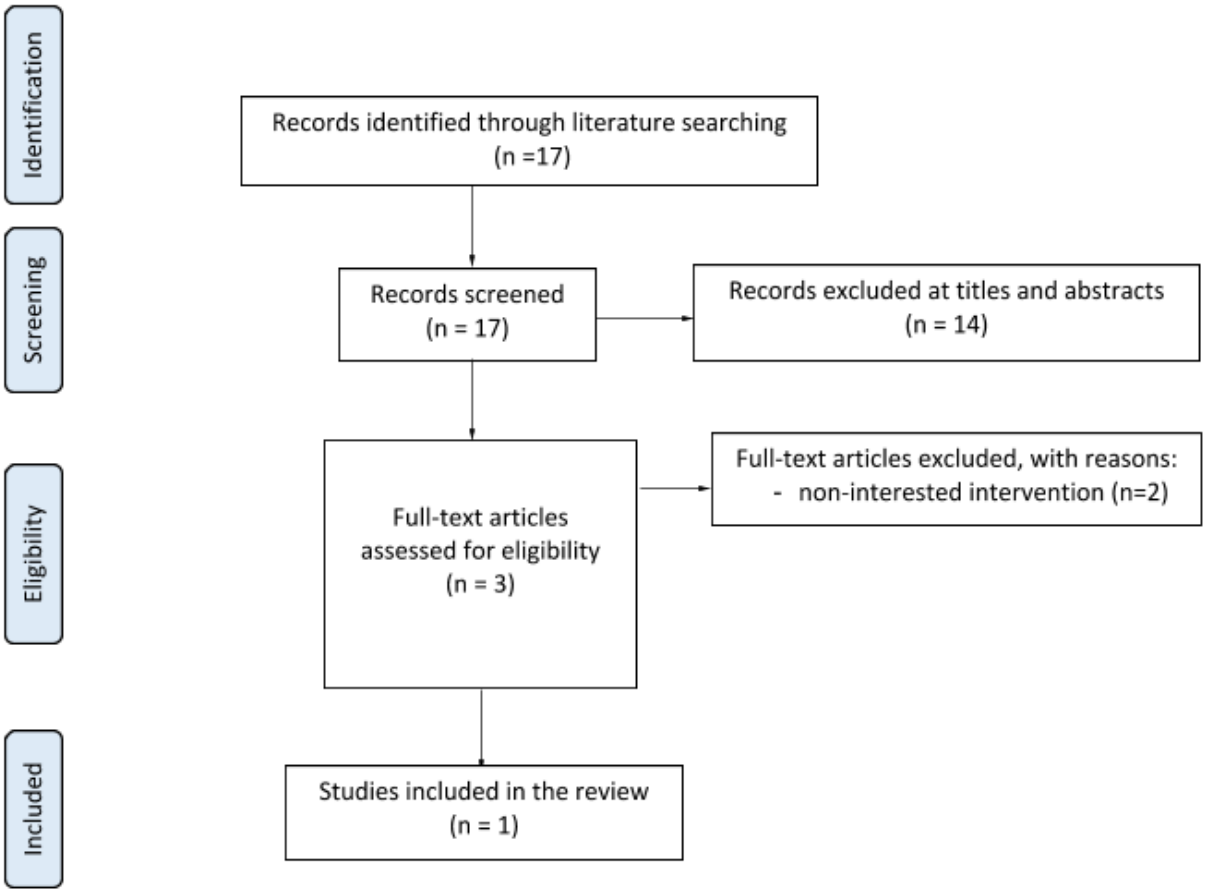
Country	Who is being tested based on their national testing policy?	Standard test	Is IgG and IgM approved in their country for market entry?	Reference
PHL	symptomatic patients only	rRT-PCR assay	No	Philippine Society for Microbiology and Infectious Diseases. (2020). Interim guideline on the clinical management of patients with suspected and confirmed 2019-novel Coronavirus (COVID-19) Acute Respiratory Disease ver. 2.0. (March)
International (WHO)	symptomatic patients only	RT-PCR	-	World Health Organization. (2020). *Operational considerations for case management of COVID-19 in health facility and community: interim guidance 2*.
Canada	symptomatic patients only	RT-PCR	did not mention	Government of Canada. (2020). Coronavirus disease (COVID-19): For health professionals - Canada.ca. Retrieved March 24, 2020, from https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals.html
United States (CDC)	symptomatic patients only	RT-PCR	did not mention	United States Center for Disease Control and Prevention. (2020). Interim Guidance: Healthcare Professionals 2019-nCoV | CDC. Retrieved March 24, 2020, from https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fclinical-criteria.html United States Centers for Disease Control and Prevention. (2020). Testing for COVID-19 | CDC. Retrieved March 24, 2020, from https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/testing.html

European Union	symptomatic patients AND 14 days prior to symptom onset, history of travel or residence in country/area reporting local transmission OR have been in close contact with a confirmed case OR requiring hospitalization and no other etiology that fully explains clinical presentation	RT-PCR	Multiple lateral flow kits are registered by CE-IVD.	European Center for Disease Control. (2020, February 25). Algorithm for the management of contacts of probable or confirmed COVID-19 cases. Retrieved March 24, 2020, from https://www.ecdc.europa.eu/en/publications-data/algorithm-management-contacts-probable-or-confirmed-covid-19-cases European Center for Disease Control. (2020, March 2). Case definition and European surveillance for COVID-19, as of 2 March 2020. Retrieved March 24, 2020, from https://www.ecdc.europa.eu/en/case-definition-and-european-surveillance-human-infection-novel-coronavirus-2019-ncov Foundation for Innovative New Diagnostics. (n.d.). SARS-CoV-2 diagnostic pipeline - FIND. Retrieved March 24, 2020, from https://www.finddx.org/covid-19/pipeline/
United Kingdom	Symptomatic patients only	RT-PCR	did not mention	Public Health England. (2020). COVID-19: investigation and initial clinical management of possible cases - GOV.UK. Retrieved March 24, 2020, from https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wn-cov-infection#action-to-take-if-inpatient-definition-is-met UK National Health Service. (2020). Coronavirus (COVID-19) - NHS. Retrieved March 24, 2020, from https://www.nhs.uk/conditions/coronavirus-covid-19/
Australia (ANZICS) - Australia and New Zealand Intensive Care Society	symptomatic patients only	RT-PCR	did not mention	The Australian and New Zealand Intensive Care Society. (2020). *The Australian and New Zealand Intensive Care Society (ANZICS) COVID-19 Guidelines Version 1*. Retrieved from https://www.health.nsw.gov.au/Infectious/diseases/Documents/anzics-covid-19-guidelines.pdf

AUSTRALIA (CDNA)-Communicable Disease Network Australia	symptomatic patients only	RT-PCR	did not mention	Communicable Disease Network Australia. (2020). CDNA National Guidelines for Public Health Units. Retrieved March 24, 2020, from https://www1.health.gov.au/internet/main/publishing.nsf/Content/7A8654A8CB144F5FCA2584F8001F91E2/$File/interim-COVID-19-SoNG-v2.2.pdf
South Korea	**asymptomatic, mild**, and symptomatic patients	RT-PCR	did not mention	Dudden, A., & Marks, A. (2020, March 20). South Korea took rapid, intrusive measures against Covid-19 – and they worked | Alexis Dudden and Andrew Marks | Opinion | The Guardian. Retrieved March 24, 2020, from The Guardian website: https://www.theguardian.com/commentisfree/2020/mar/20/south-korea-rapid-intrusive-measures-covid-19 Won, J., Lee, S., Park, M., Kim, T. Y., Park, M. G., Choi, B. Y., … Lee, C. J. (2020). Development of a Laboratory-safe and Low-cost Detection Protocol for SARS-CoV-2 of the Coronavirus Disease 2019 (COVID-19). Experimental Neurobiology. doi: 10.5607/en20009 Yamey, G. (2020, March 17). What the U.S. Needs to do to Follow South Korean Model | Time. Retrieved March 24, 2020, from TIME website: https://time.com/5804899/u-s-coronavirus-needs-follow-s-korea/
China	symptomatic patients only	RT-PCR	did not mention	The First Affiliated Hospital, Z. U. S. of M. (2020). *Handbook of COVID-19 Prevention and Treatment Compiled According to Clinical Experience*. Zhejiang Province, China.
Singapore	symptomatic patients and health workers	RT-PCR	did not mention	Fisher, D. (2020, March 18). Why Singapore's coronavirus response worked – and what we can all learn. Retrieved March 24, 2020, from The Conversation website: https://theconversation.com/why-singapores-coronavirus-response-worked-and-what-we-can-all-learn-134024

Japan	symptomatic patients only	RT-PCR	did not mention	Lindsay, D. S., & Nosek, B. A. (2020). *Reporting criteria of Novel Coronavirus 2019 infection in Japan*. *21*(1), 1–9. Watanabe, H. R. (2020, March 18). Coronavirus in Japan: why is the infection rate relatively low? Retrieved March 24, 2020, from https://theconversation.com/coronavirus-in-japan-why-is-the-infection-rate-relatively-low-133648
Thailand	symptomatic patients only, and patients with recent travel history to crowded spots such as stadiums.	RT-PCR	did not mention	The Star. (2020, March 17). Thailand offers free Covid-19 tests for special cases | The Star Online. Retrieved March 24, 2020, from The Star website: https://www.thestar.com.my/news/regional/2020/03/17/thailand-offers-free-covid-19-tests-for-special-cases Royal Thai Embassy. (2020). COVID-19 Situation in Thailand. Retrieved March 24, 2020, from https://thaiembdc.org/covid-19inthailand/ *Main site of ministry of public health not accessible.

Appendix 2. Selection of Included studies (Search for clinical accuracy studies)



Appendix 3. Description of Studies

3.1 Characteristics of Included Study

Author, Year, Title	Study design	Country	PICO	Main findings and conclusion	Reference
Li et al. (2020) Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis	Non-randomized trial	China	P: Patients with suspected case of COVID-19 I: IgG/IgM RDT kits C: *no comparator specified* O: Turnaround time, Sensitivity, Specificity, detection consistency	Main findings: Turnaround time: 15 minutes Reported clinical sensitivity: 88.66% Reported clinical specificity: 90.63% Detection consistency: 100% Detection limit: Not determined yet. Conclusion: The IgM-IgG combined assay has better utility and sensitivity compared with a single IgM or IgG test. It can be used for the rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic, in hospitals, clinics, and test laboratories.	https://doi.org/10.1002/jmv.25727

3.2 Characteristics of Excluded Studies

Author Year	Reason for exclusion
Guo, L. et. al. (2020)	Intervention used in the study was ELISA and not a rapid IgG/IgM diagnostic kit
Pang, J. et. al. (2020).	Interventions included in the systematic review were all RT-PCR.

Appendix 4. Selection of Included studies (Search for cost-effectiveness studies)