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 asymptomatic individuals scheduled for non-urgent, non-emergent surgery, should RT-PCR and clinical risk assessment vs clinical risk assessment alone be done to screen for COVID-19?**

Review by: Marie Gene D. Cruz-Tantoco, MD, Michelle Cristine Miranda, MD, Maria Teresa S. Tolosa MD D Clin Epi, Evalyn A. Roxas, MD, MPH, Donna Isabel S. Capili, MD, Marissa M. Alejandria, MD, MSc

RECOMMENDATIONS

Recommendations	Certainty of Evidence	Strength of Recommendation
Among asymptomatic individuals scheduled for non-emergent/non-urgent surgery, we suggest using clinical risk assessment alone to screen for COVID-19.	Very low	Weak
Among asymptomatic individuals scheduled for non-emergent/non-urgent surgery who have been diagnosed to have COVID-19 within the last 90 days, we suggest against the use of SARS-CoV-2 RT-PCR.	Very low	Weak

Consensus Issues

1) The panel emphasized that clinical risk assessment should include asking about history of COVID-19 symptoms and a possible history of exposure to SARS-CoV-2.
2) There are certain important qualifiers and potential confounders that the review did not find evidence for and hence were not discussed, including the vaccination status of the patient, associated comorbidities, immunocompromised status, and the length and type of operative procedure, among others.
3) The panel acknowledged the low sensitivity of clinical risk assessment alone in screening for COVID-19 cases for asymptomatic individuals but the panel pointed out the delays and costs incurred when requiring RT-PCR testing prior to non-emergent/non-urgent surgery. The panel also pointed out that this recommendation is subject to change if there should be a significant increase of COVID-19 infections among the population.

KEY FINDINGS

- This updated review contains four observational studies as indirect evidence sources for diagnostic accuracy and postoperative outcomes. Three new observational studies were included, in addition to one study mentioned from the previous review. We excluded two studies from the earlier version due to very serious indirectness issues.
- Based on three observational studies, clinical risk assessment had low sensitivity ranging from 0.38-0.50, compared to RT-PCR test as the gold standard for detecting COVID-19 infection. Four cross-sectional studies revealed that clinical risk assessment or symptom screening questionnaires have variable specificity range of 0.62-1.00. In terms of postoperative outcomes, two observational studies showed that patients who tested positive for COVID-19 had significantly increased risk of postoperative all-cause mortality compared to those who were COVID-19 negative preoperatively.
- The overall certainty of evidence regarding the sensitivity and specificity of risk assessment questionnaires and all-cause mortality outcome was deemed to be very low. Serious risk of bias

was noted from the a) subjective interpretation of the index test (risk assessment or symptom questionnaire) and b) study methodology (observational), where the clinical outcomes were concerned. Moreover, the small sample size and event rates in one outcome contributed to serious imprecision issues.

- Lastly, issues of indirectness were also noted since patients for semi-urgent procedures were recruited in two studies, and outcomes on unscreened patients were uninvestigated in all four studies.

PREVIOUS RECOMMENDATIONS
As of 09 April 2021

We recommend using both clinical risk assessment and RT-PCR* to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery. *(Very low certainty of evidence; Strong recommendation)*

We recommend using both clinical risk assessment and Antigen-Rapid Diagnostic Test (Ag-RDT)** to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery when RT-PCR testing is not available or when prolonged turnaround time is a concern. *(Very low certainty of evidence; Strong recommendation)*

**Always use high-risk PPE regardless of RT-PCR or Ag-RDT test results in areas with prevalence of 1% or higher*
***Ag-RDT should have a Sn of 80% and Sp of 97%*

Consensus Issues
Despite the very low quality of evidence, the majority voted to strongly recommend the use of both RT-PCR testing and clinical risk assessment to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery primarily due to the potential impact of a false negative result on the safety of the patient and health care staff involved as well as on the infection control processes of hospitals. RT-PCR was also recommended as it is now readily available in most hospitals. However, a panelist suggested that RT-PCR and PPE should only be conditionally recommended in areas with prevalence rates of 1% or higher.

The specification of the sensitivity and specificity for the Ag-RDT was the reason for the strong recommendation on the use of clinical risk assessment and Ag-RDT to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery when RT-PCR testing is not available. However, other panelists were concerned about the availability of antigen tests that would meet the set specification in terms of sensitivity and specificity

INTRODUCTION

The COVID-19 pandemic has led to postponement of non-urgent and non-emergent surgeries in institutions across the globe. Asymptomatic COVID-19 patients undergoing surgery are at a higher risk of postoperative mortality and ICU admission compared to those without COVID-19 [1-3]. The proportion of asymptomatic COVID-19 cases was reported to be 17.9% [4]. Hence, ascertaining the COVID-19 status of asymptomatic surgical candidates informs decisions to prevent viral transmission and reduce postoperative complications.

Recommendations for routine RT-PCR testing have been made for elective surgical candidates suspected of COVID-19 based on the availability of the test, turnaround time, availability of PPE, and disease prevalence [5]. Its results also depend on sampling technique, specimen handling, and timing of specimen collection from symptom onset [6,7]. False-negative rates for RT-PCR were estimated to reach as high as 16% [8].

Clinical risk assessment includes determining a history of close contact with a confirmed COVID-19 case (i.e., within 6 feet for a total of 15 minutes or more) and evaluating symptoms. Risk is also considered high if a person has taken part in activities where physical distancing is difficult to maintain, such as travel, attending large social or mass gatherings, or being in crowded indoor settings [9]. Its diagnostic performance for screening asymptomatic surgical candidates remains to be determined.

REVIEW METHODS

A comprehensive search on PubMed and Cochrane CENTRAL was done with the following search terms using our PICO: “COVID-19 testing”, “preoperative”, “risk assessment”, “symptom screening”, “COVID-19

testing", "RT-PCR". We also searched for preprints on MedRxiv, and Biorxiv and the reference lists of identified articles. The updated search strategy was done on October 30, 2022 (Appendix 1).

The following inclusion criteria were used for this review:

- Study design: randomized controlled trials, controlled clinical trials, observational studies
- Population: asymptomatic individuals scheduled for elective or non-urgent/non-emergency surgery
- Exposure: clinical risk assessment or other pre-operative COVID-19 testing methods
- Outcome: screening for COVID-19, diagnostic accuracy, postoperative outcomes

Appraisal of the included studies was done using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) and Newcastle-Ottawa Scale for nonrandomized studies (Appendix 2). RevMan software version 5.4 was used to generate the appraisal table and forest plots. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to evaluate the quality of evidence.

RESULTS

Characteristics of included studies

We found four observational studies (3 retrospective, 1 prospective) on adult patients (age 18 and above) about to undergo non-emergent surgery or endoscopic procedures who were subjected to clinical risk assessment or symptom screening prior to the planned procedures [10-13]. Characteristics of the included studies are available in Appendix 3.

The four cross-sectional studies (n=1756) involved symptom or risk-based screening for COVID-19 using questionnaires. All patients underwent RT-PCR testing (reference standard) regardless of the presence or absence of symptoms and exposure. However, in one prospective study by Stessel 2021, chest CT scan was also done in all patients to screen for the ground-glass opacities, the presence of which was considered COVID-19 diagnosis in the study [10]. Two studies recruited patients about to undergo semi-urgent procedures, while the rest of the three studies involved elective or non-urgent/non-emergent procedures. Endoscopic procedures and orthopedic and gynecologic surgeries were included in the studies. Outcomes of interest were prevalence of COVID-19 infection and diagnostic accuracy of screening questionnaires, post-operative COVID-19 infection, and mortality.

Diagnostic accuracy outcomes

Outcomes from three observational studies showed that the sensitivity of clinical risk assessment or symptom screening questionnaire ranged from 0.38-0.50 (95% CI 0.27-0.73 to 0.09-0.76). On the other hand, specificity of this test ranged from 0.62-1.00 (95% CI 0.97-1.00 to 0.76-0.92) based on 3 retrospective and 1 prospective cross-sectional studies (Appendix 5). Pooling of outcomes was not done due to variability of screening tests and questionnaires used by different studies.

Post-operative COVID-19 infection

The study by Areeruk (2021) followed up all patients postoperatively at 2 weeks for possible complications. None of the patients developed postoperative complications or COVID-19 infection during the follow up period.

All-cause Mortality

Two observational studies reported mortality outcomes among patients who underwent testing. COVID-19 positive patients were seen to have increased risk of postoperative all-cause mortality compared to patients who tested negative for COVID-19 (RR 16.06, 95% CI 2.19-117.96, I^2=30%) (Appendix 5).

Certainty of evidence

GRADE approach was used to analyze the overall quality of evidence (Appendix 4). Evidence for the sensitivity and specificity of risk assessment questionnaires was deemed to be very low due to serious risk of bias since the interpretation of the index test (risk assessment or symptom questionnaire) is subjective, and indirectness issues since two studies involved patients undergoing semi-urgent or emergency

procedures and one study included CT scan as another test to confirm COVID-19 diagnosis. The evidence for post-operative COVID-19 infection was also of very low quality due to 1) risk of bias issue from study methodology (observational), 2) imprecision issue from small sample size and event rates, and 3) indirectness issue for the lack of evidence on unscreened groups. Lastly, the evidence on all-cause mortality was also deemed to be of very low quality from issues on risk of bias and indirectness as mentioned.

RECOMMENDATIONS FROM OTHER GROUPS

The Centers for Disease Control and Prevention (CDC) (dated 28 Sep 2022) has general recommendations regarding COVID-19 testing in its latest guidance for healthcare workers about COVID-19. Diagnostic testing using a viral test (RT-PCT or nucleic acid amplification tests [NAAT], antigen or other diagnostic tests) are recommended for 1) persons with signs and symptoms consistent with COVID-19, and 2) asymptomatic persons with recent known or suspected exposure to the virus. To determine new infection among persons who were exposed to COVID-19 but recently tested positive within the past 30-90 days, antigen test should be done. However, there was no mention on particular screening testing prior to conducting procedures or surgeries in healthcare facilities [9].

The Infectious Disease Society of America (IDSA) (dated 23 Dec 2020) suggests RT-PCR testing for asymptomatic individuals without known exposure to COVID-19 who are undergoing major time-sensitive surgeries (i.e., medically necessary surgeries that need to be done within three months). No recommendation was mentioned regarding COVID-19 screening for elective surgeries. However, the Society mentioned that deferral of non-emergent surgeries for patients who test positive for COVID-19 should be considered to minimize possible poor outcomes [14].

Similarly, the American Society of Anesthesiologists (ASA) and Anesthesia Patient Safety Foundation (APSF) (dated 22 Feb 2022) made a joint recommendation that all patients should be screened for COVID-19 symptoms prior to coming to the health care facility. Additionally, patients about to undergo non-emergent surgery should be tested for COVID-19 via RT-PCR [15].

The Philippine Society for Microbiological and Infectious Diseases (PSMID) and Philippine Hospital Infection Control Society (PHICS) (dated 26 May 2020) recommend COVID-19 clinical risk assessment for patients about to undergo surgery, and if available, RT-PCR. Accessibility, turnaround time, and cost-effectiveness (cost of RT-PCR vs. cost of PPE) are important considerations when RT-PCR is to be requested [5].

Other local and international groups such as American College of Surgeons (ACS) (dated 17 Apr 2020), Philippine College of Surgeons (PCS) (dated 20 Apr 2020) and Philippine Academy of Ophthalmology (dated Nov 2020) recommend preoperative RT-PCR testing may be considered for patients for planned procedures [16-18].

ONGOING STUDIES AND RESEARCH GAPS

Currently, there are no ongoing randomized clinical trials on this topic.

ADDITIONAL CONSIDERATIONS FOR EVIDENCE TO DECISION (ETD) PHASE

COST

There are no economic evaluation studies available on clinical risk assessment for COVID-19 diagnosis. However, in terms of cost, RT PCR test can be availed at around ₱1,500-5,000 through the Philippine Red Cross (PRC) testing facility [19]. PRC offers outpatient RT PCR test using either nasopharyngeal swab or saliva samples through its satellite testing facilities nationwide. In terms of Philippine Health Insurance Corporation (PhilHealth) coverage, the agency announced in a circular last November 30, 2021, that it shall provide coverage for PCR testing ranging from ₱800-2,800 for plate-based, and ₱500-2,450 for cartridge-based RT PCR tests [20]. On the other hand, both risk assessment and symptom screening do not require

additional resources aside from printed or digital questionnaires. Screening may also be done via telephone call.

PATIENT'S VALUES AND PREFERENCE, EQUITY, ACCEPTABILITY, AND FEASIBILITY

No studies were found on patient's values, preference, equity, acceptability, and feasibility on the use of clinical risk assessment for COVID-19 screening and diagnosis.

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APPENDICES

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)					The COVID-19 pandemic has led to postponement of non-urgent and non-emergent surgeries in institutions across the globe. Asymptomatic COVID-19 patients undergoing surgery are at a higher risk of postoperative mortality and ICU admission compared to those without COVID-19 [1-3]. The proportion of asymptomatic COVID-19 cases was reported to be 17.9% [4]. Hence, ascertaining the COVID-19 status of asymptomatic surgical candidates informs decisions to prevent viral transmission and reduce postoperative complications.
Benefits	Large (N=3)	Moderate (N=2)	Small	Varies	Uncertain		
Harms	Large (N=5)	Moderate	Small	Uncertain			Patients who are screened and test positive (RT PCR) for COVID-19 had higher postoperative all-cause mortality risk.
Balance of Benefits and Harms	Favors the use of the comparison (N=1)	Probably favors the use of comparison (N=3)	Does not favor either the intervention or the comparison	Probably favors the intervention (N=1)	Favors the intervention	Don't know	
Certainty of Evidence	High	Moderate	Low (N=2)	Very Low (N=3)			Overall certainty of evidence sensitivity and specificity of risk assessment questionnaires was deemed to be very low due to serious risk of bias from subjective interpretation of the index test (risk assessment or symptom questionnaire), and indirectness issues since two studies involved patients undergoing semi-urgent or emergency procedures and one study included CT scan as another test to confirm COVID-19 diagnosis.

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
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			
Resources Required	Don't Know	Large cost (N=1)	Moderate Cost (N=2)	Negligible cost or savings (N=1)	Moderate savings	Large Savings (N=1)	Only printed/digital questionnaires are the resources required to conduct clinical risk assessment. It may even be conducted via telephone call.
Certainty of evidence of required resources	No included studies (N=2)	Very low	Low (N=2)	Moderate (N=1)	High		There are no economic evaluation studies available on clinical risk assessment for COVID-19 diagnosis. However, in terms of cost, RT PCR test can be availed at around PhP 1,500 to 5,000 through the Philippine Red Cross (PRC) testing facility [19]. Available nationwide through its satellite testing facilities, the PRC offers outpatient RT PCR test using either nasopharyngeal swab or the less invasive saliva testing. On the other hand, both risk assessment and symptom screening do not require additional resources aside from printed or digital questionnaires. Screening may also be done via telephone call.
Cost effectiveness	No included studies (N=2)	Favors the comparator (N=1)	Does not favor either criteria or the comparator	Probably favors the intervention (N=1)	Favors intervention (N=1)		
Equity	Don't Know	Probably Reduced (N=1)	Reduced (N=2)	Probably Increased (N=1)	Probably No impact (N=1)	Varies	In terms of Philippine Health Insurance Corporation (PhilHealth) coverage, the agency announced in its circular last November 30, 2021 that it shall provide coverage for PCR testing ranging from ₱800-2,800 for plate-based, and ₱500-2,450 for cartridge-based RT PCR tests.
Acceptability	Don't Know	No	Probably No	Yes (N=1)	Probably yes (N=3)	Varies (N=1)	
Feasibility	Uncertain	No	Probably No	Yes (N=4)	Probably yes (N=1)	Varies	

Appendix 2: Search Strategy

Table 2. Search Strategy per database

DATABASE	SEARCH STRATEGY / SEARCH TERMS	DATE OF SEARCH	RESULTS	
			Yield	Eligible
Medline	(risk assessment OR symptom screening) AND (preoperative OR preprocedure)) AND ("COVID-19 testing" [Mesh])	October 20, 2022	147	14
CENTRAL	P: Elective Surgery I: Risk assessment C: COVID-19 RT-PCR testing	October 20, 2022	0	0
Medrxiv.org	COVID-19 surgery risk assessment Filters: March 1, 2021 to October 30, 2022	October 20, 2022	261	0
Biorxiv.org	COVID-19 surgery risk assessment Filters: March 1, 2021 to October 30, 2022	October 20, 2022	275	0

Appendix 3: Quality Assessment of Included Studies

Table 3. QUADAS-2 Tool Appraisal

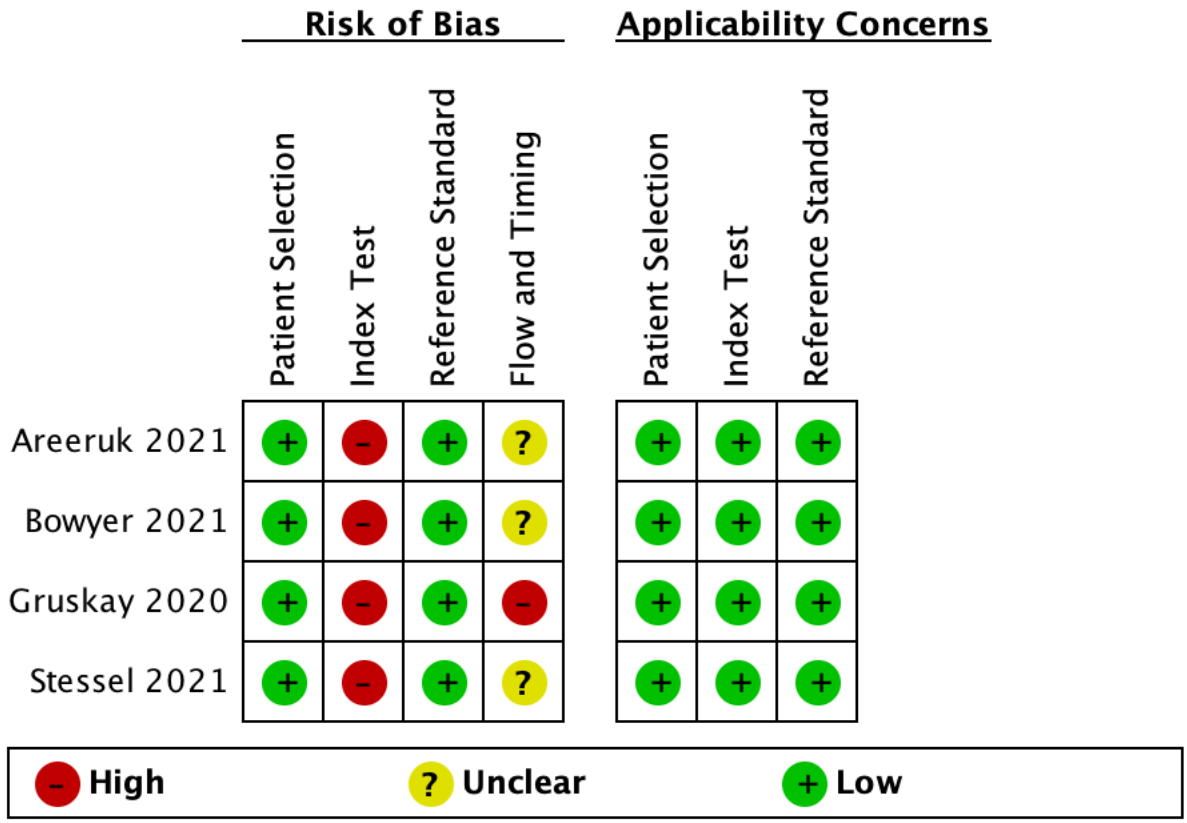

Table 4. Newcastle-Ottawa Scale Appraisal

Study ID	Selection				Comparability	Outcome		Total
	Representative of the cases	Sample size	Non-response rate	Ascertainment of screening or surveillance tool	Potential confounders	Assessment of outcome	Statistical test	
Gruskay 2020	*	-	-	*	-	*	*	**** (4) (poor)
Stessel 2021	*	-	-	*	-	*	*	**** (4) (poor)

Appendix 4: Characteristics of Included Studies

Table 5. Summary of study characteristics

Study ID	Setting	Index Test	Population	Sample Size	Reference standard
Gruskay 2020	USA	Symptom-based screening	adult symptomatic and asymptomatic patients who had preoperative RT-PCR testing prior to orthopedic surgery	116	RT-PCR
Stessel 2021	Belgium	Symptom-based screening	adult patients admitted for pre-procedural consultation (2 days before semi-urgent procedure)	528	RT-PCR CT scan
Areeruk 2021	Thailand	Symptom-based screening	adult patients for elective or emergency gynecologic surgeries	129	RT-PCR
Bowyer 2021	USA	ASGE preprocedure COVID-19 Risk/symptom screening questionnaire	patients 18 to 85 years scheduled to undergo endoscopic procedure	1000	RT-PCR

Appendix 5: GRADE Evidence Profiles

Question: Should Risk Assessment + RT PCR vs Risk Assessment alone be used to diagnose COVID-19 in asymptomatic patients for non-urgent and non-emergent surgery?

Sensitivity	0.38 to 0.50
Specificity	0.62 to 1.00

Prevalences	1%	5%	

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 of1%	pre-test probability of5%	
True positives (patients with COVID-19)	4 studies 40 patients	cross-sectional (cohort type accuracy study)	serious[a]	very serious[b, c]	not serious	not serious	none	4 to 5	19 to 25	⊕◯◯◯ Very low
False negatives (patients incorrectly classified as not having COVID-19)								5 to 6	25 to 31	
True negatives (patients without COVID-19)	4 studies 1716 patients	cross-sectional (cohort type accuracy study)	serious[a]	very serious[b, c]	serious[d]	not serious	none	614 to 990	589 to 950	⊕◯◯◯ Very low
False positives (patients incorrectly classified as having COVID-19)								0 to 376	0 to 361	

Explanations

a. The interpretation of the index test may have introduced bias since symptom assessment is subjective
b. Studies compared risk assessment/symptom screening (index test) with RT PCR (reference standard) and not risk assessment + RT PCR vs risk assessment alone as in the clinical question
c. Two studies included semi-urgent and emergent procedures.
d. One study by Stessel 2021 used CT scan as another test to confirm COVID-19 diagnosis
e. Heterogeneous outcome

Risk Assessment + RT PCR compared to Risk Assessment alone for COVID-19 screening in asymptomatic patients for non-urgent and non-emergent surgery

Bibliography:

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With Risk Assessment alone	With Risk Assessment + RT PCR	Relative effect (95% CI)	Risk with Risk Assessment alone	Risk difference with Risk Assessment + RT PCR
Post-operative COVID-19 infection											
116 (1 observational study)	not serious	not serious	serious[a]	serious[b]	none	⊕◯◯◯ Very low	The study by Areeruk (2021) followed up all patients postoperatively at 2 weeks for possible complications. None of the patients developed postoperative complications or COVID-19 infection during the follow up period.				
Mortality											
644 (2 observational studies)	not serious	not serious	serious[a]	not serious	none	⊕◯◯◯ Very low	2/606 (0.3%)	4/38 (10.5%)	**RR 16.06** (2.19 to 117.96)	3 per 1,000	**50 more per 1,000** (from 4 more to 386 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Not a screening RCT, only included patients who were screened for symptoms/risk

b. Single study with small sample size

Appendix 6: Forest Plot

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Areeruk 2021	0	0	0	129	Not estimable	1.00 [0.97, 1.00]
Bowyer 2021	3	119	5	873	0.38 [0.09, 0.76]	0.88 [0.86, 0.90]
Gruskay 2020	5	13	7	74	0.42 [0.15, 0.72]	0.85 [0.76, 0.92]
Stessel 2021	10	191	10	317	0.50 [0.27, 0.73]	0.62 [0.58, 0.67]

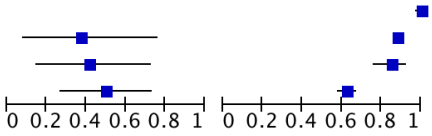

Figure 1. Forest plot of diagnostic accuracy of Risk Assessment or Symptom Screening Questionnaires in diagnosing COVID-19.

Study or Subgroup	COVID-19 positive Events	COVID-19 positive Total	COVID-19 negative Events	COVID-19 negative Total	Weight	Risk Ratio M-H, Random, 95% CI
Gruskay 2020	3	18	2	98	69.1%	8.17 [1.47, 45.48]
Stessel 2021	1	20	0	508	30.9%	72.71 [3.05, 1732.38]
Total (95% CI)		**38**		**606**	**100.0%**	**16.06 [2.19, 117.96]**
Total events	4		2			

Heterogeneity: $Tau^2 = 0.73$; $Chi^2 = 1.43$, df = 1 (P = 0.23); $I^2 = 30\%$
Test for overall effect: Z = 2.73 (P = 0.006)

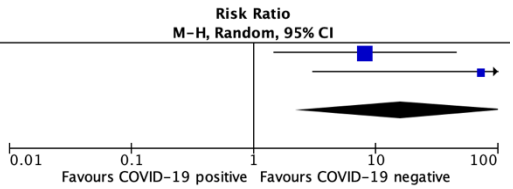

Figure 2. Forest plot on all-cause mortality between COVID-19 positive and negative patients