CHEST X-RAY

RECOMMENDATIONS

We suggest against the use of chest x-ray to diagnose COVID-19 infection among asymptomatic individuals *(Very low quality of evidence; Conditional recommendation).*

We suggest chest x-ray to facilitate rapid triage, infection control and clinical management among any of the following *(Very low quality of evidence; Conditional recommendation)*:

- patients with mild features of COVID 19 at risk for progression
- patients with moderate to severe features of COVID 19
- patients with symptoms of at least 5 days duration

Consensus Issues

The use of chest X-ray to diagnose COVID-19 infection among asymptomatic individuals was not suggested due to the very low quality of evidence related to its diagnostic accuracy. High heterogeneity across studies was also observed and the studies reviewed did not perform subgroup analysis according to severity of COVID-19. However, chest x-ray is still suggested for specific instances as there would be a high yield in detecting significant pulmonary abnormalities in these settings.

EVIDENCE SUMMARY

Should Chest x-ray be done to diagnose COVID-19 among suspected patients?

Evidence Reviewers: Maria Cristina Z. San Jose, MD and Valentin C. Dones, PTRP, MSPT, PhD

Key Findings

CXR typically shows bilateral and diffuse involvement with ground-glass opacities and consolidation in the lung periphery, and is only moderately sensitive and moderately specific in the diagnosis of COVID-19 in suspected cases. Very low certainty evidence from 9 observational studies showed that the sensitivity of CXR ranged from 56% to 94%, while its specificity ranged from 60% to 89%. The pooled sensitivity for CXR was 74% (95%CI 59 to 85%) while pooled specificity was 76% (95%CI 67 to 83%). Significant heterogeneity was observed across studies, possibly because of a number of factors including patients' characteristics, timing of CXR in relation to symptom onset, definition of index test positivity and experience of CXR readers.

Introduction

Current COVID-19 radiological literature is dominated by chest computed tomography (CT). Due to its higher sensitivity [1,2] compared to chest x-ray (CXR), chest CT is often used as a first-line diagnostic exam. CT scan suites that are dedicated solely for suspected COVID-19 patients have been set up in some hospitals. However, this may not be accessible or feasible in many local hospitals and places a higher demand on health facilities because of the disinfection protocols required after each procedure. In contrast, CXR is more ubiquitous, readily available, and is

associated with 30-70% lower radiation exposure. CXR also provides faster results compared to reverse transcription-polymerase chain reaction (RT-PCR) which has turnaround times ranging from hours to several days. However, data on specific CXR findings considered diagnostic of COVID-19 remain limited. This review describes the percentage of normal and abnormal CXR findings, the frequency of CXR abnormalities among laboratory confirmed COVID-19 patients, and the diagnostic performance of CXR compared to RT-PCR as the reference standard.

Review Methods

We included observational studies, randomized controlled trials (RCTs) and systematic reviews of observational studies that evaluated the diagnostic accuracy of chest radiography for diagnosing COVID-19. A positive RT-PCR test for SARS-COV2 infection from any manufacturer, in any country, and any source of sample such as nasopharyngeal or oropharyngeal swabs or aspirates was used as reference standard. To obtain information on common CXR findings, we also included case reports.

A comprehensive literature search was performed using combined subject headings and keywords[1] on April 5, 2021 in the following electronic databases: MEDLINE, EBSCO (CINAHL plus with full-text) and ScienceDirect. We excluded articles published before 2020, non-English articlels, had no available full-text reports, or did not have sufficient data to produce estimates of test accuracy or provide 2x2 data.

Results

Characteristics of included studies

Diagnostic accuracy data was reported in 9 observational studies (6 retrospective cohort, 3 cross sectional studies) [13-14, 16, 19-24]. The definition of a positive CXR result varied considerably across studies. Most studies used typical abnormalities seen in radiographs of patients with COVID-19 pneumonia [12-14,16,22-23], two studies [19,20] used a formal scoring system (i.e. British Society of Thoracic Imaging (BSTI) reporting template), and one used an unvalidated Likert scale based on a proposed standard for reporting of chest CT scan [21]. The timing of CXR in relation to RT-PCR was also variable, ranging from within 12 hours to 30 days from the reference test.

Thirty-one observational studies (29 cross-sectional, 2 case series) from 15 countries[2] have described chest x-ray findings of adults (n = 3341) who tested COVID-19 positive based on RT-PCR [3–18]. Cough and fever were common presenting symptoms of COVID-19 patients included in these studies. Three studies focused only on critically ill patients [6,7,9] and one was conducted in an ambulatory care setting [11]. Only 3 studies reported progress of lung abnormalities on serial CXR [4,8-9]. Three studies graded severity of findings [4, 11-12].

[1]Keywords 1: “Coronavirus Infections” [Mesh} OR “Coronavirus” [Mesh] OR coronavirus OR novel coronavirus OR NCOV or “COVID-19” [Supplementary Concept} OR covid19 OR covid 19 OR covid-19 OR “severe acute respiratory syndrome coronavirus 2” [Supplementary Concept] OR severe acute respiratory syndrome coronavirus 2 OR SARS2 OR SARS 2 OR SARS COV2 OR SARS COV 2 OR SARS-COV-2
Keywords 2: chest x-ray OR chest x-ray OR Mass chest x-ray OR Mass chest x-ray
Keywords 3: Cough OR flu OR acute respiratory syndrome OR respiratory distress syndrome OR severe acute respiratory syndrome OR SARS virus

[2] China, Italy, Australia, South Korea, Germany, France, India, Hongkong Taiwan, Vietnam, Canada, Japan, Nepal, Thailand, USA

Overall quality of evidence

The body of evidence for diagnostic accuracy was assigned an overall GRADE rating of very low. Serious risk of bias was noted, with unclear data on all QUADAS-2 domains (Patient Selection, Index Test, Reference Standard, and Flow and Timing) in at least 50% of the studies. Very serious inconsistency was noted due to high heterogeneity. Wide confidence intervals were seen in three studies [14,21,23].

Outcomes

Diagnostic performance of CXR

The sensitivity of CXR ranged from 56% to 94% (9 studies, n=3659) [12-14, 16, 19–23] and the specificity ranged from 60% to 89% (9 studies, n=3659) [12–14,19–23]. The pooled sensitivity for CXR was 74% (95%CI 59 to 85%) while pooled specificity was 76% (95%CI 67 to 83%). Significant heterogeneity was observed across studies, possibly because of a number of factors including patients' characteristics, timing of CXR in relation to symptom onset, definition of index test positivity, and experience of CXR readers.

One study that investigated the effect of timing of CXR on sensitivity for COVID-19 detection showed low sensitivity at 55% if taken ≤2 days from symptom onset and increased to 79% >11 days after symptom onset [16]. Sensitivity similarly was higher among patients with longer interval from symptom onset to imaging (76 % if > 5 days and 37% if < 5 days) [13]. More extensive years of training and experience of radiographers in interpreting images (> 10 years) was also observed to enhance the diagnostic performance of CXR [24].

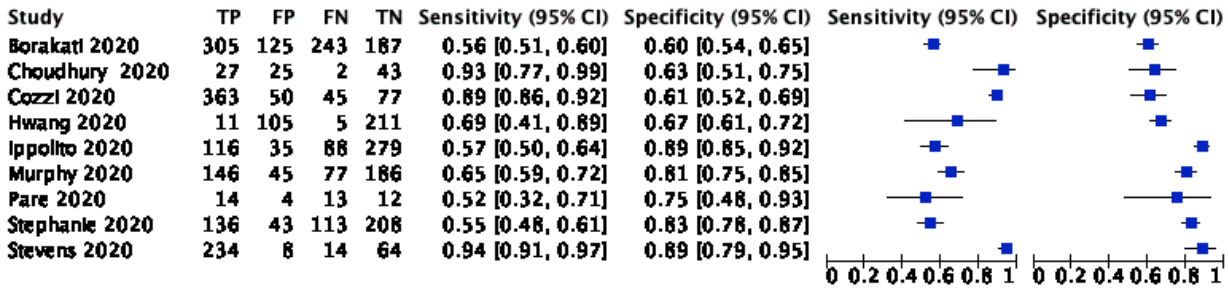

Figure 1. Forest plots showing the sensitivity and specificity of chest x-ray for diagnosing COVID-19.

Common findings and distribution on initial CXR

Table 1 summarizes the abnormalities found on chest x-rays in individuals with COVID-19. No single CXR feature was considered specific and diagnostic of COVID-19 pneumonia [25]. Abnormal findings were reported in 33-100% of patients. The most common findings were bilateral pneumonia (52.5%), ground glass opacities (46.7%), interstitial involvement (39.2%) and/or consolidation (38.5%). These occurred singly or in combination. The locations of abnormalities were often multifocal or diffuse (62%). These data have been combined from published reports and the wide estimates may be due to varying disease severity and disease duration of patients in the reports. Initial CXR have been reported to be normal at the onset but patients may later develop radiological signs of COVID-19 pneumonia.

Table 1. Summary of chest x-ray findings/abnormalities reported for individuals with COVID-19

CXR findings	No of Studies	Prevalence in studies	No. of reported cases/Total no of Patients	% of patients
Abnormal findings	12	33 – 100%	1078/1733	62.2%
Diffuse distribution	5	35 – 58%	584/934	62.5%
Bilateral pneumonia	19	21 – 89%	1440/2742	52.5%
Ground glass opacity	15	20 – 68%	455/973	46.7%
Peripheral distribution	5	21 – 62%	445/1055	42.2%
Interstitial involvement	7	4 – 71%	801/2041	39.2%
Consolidation	9	3 – 60%	664/1723	38.5%
Lower lobe distribution	9	1 – 63%	798/2130	37.5%
Unilateral pneumonia	10	6 – 37%	94/564	16.6%

Recommendations from Other Groups

The **World Health Organization (WHO)** suggests against using chest imaging for the diagnosis of COVID-19 for asymptomatic contacts of patients with COVID-19. For symptomatic patients with suspected COVID-19, WHO suggests not using chest imaging for the diagnostic workup of COVID-19 when RT-PCR testing is available with timely results. For symptomatic patients with suspected COVID-19, WHO suggests using chest imaging for the diagnostic workup of COVID-19 when: (1) RT-PCR testing is not available; (2) RT-PCR testing is available, but results are delayed; and (3) initial RT-PCR testing is negative, but with high clinical suspicion of COVID-19. Patients likely to benefit from chest imaging are those who are at higher risk of disease progression, have severe signs and symptoms on physical examination, in need of emergency procedures or urgent interventions. When choosing imaging modality, it is also important to consider that although CXR has a lower sensitivity, it is associated with lower risk of HCW infection transmission. Moreover, it is less resource intensive, has lower radiation doses compared to CT scan and is easier to repeat sequentially when monitoring disease progression [26].

Currently, the **Centers for Disease Control (CDC)** does not recommend CXR or CT for the diagnosis of COVID-19 and remarks that only viral testing remains to the specific method of diagnosis. Confirmation through viral testing is required regardless if radiologic findings is suggestive of COVID-19 [27].

A radiology decision tool for suspected COVID-19 patients has been launched by the **British Society of Thoracic Imaging** which suggests the use of CXR for those who are seriously ill (oxygen saturation <94%, National Early Warning Score (NEWS) ≥ 3) and only if clinically warranted for those in stable condition (oxygen saturation >94%, NEWS < 3) [28].

A **Multinational Consensus Statement from the Fleischner Society** provided recommendations for the use of imaging to direct management of patients with COVID-19. The Fleischner Society states that imaging is not routinely indicated as a method of screening for COVID-19 among asymptomatic individuals and patients with mild features unless they are at risk for disease progression. However, imaging is indicated for patients with moderate to severe features and has worsening respiratory status. When access to CT is limited, CXR may be preferred for COVID-19 patients except for those who have worsening respiratory features in which a CT is required [29].

Research Gaps

The included studies did not assess interrater or intrarater reliability of radiologists. Studies highlighted the findings reported for COVID-19 patients in a clinical setting with variability in CXR assessment. Most researches utilize the initial CXR findings to examine the value of chest radiography in the early diagnosis of COVID-19. Progression of findings on follow-up imaging, when performed often was not described.

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Appendix 1. Summary of Chest-ray findings among Laboratory-confirmed (RT-PCR) Patients in Observational studies

	Arentz et al. (2020) (6)	Albarello et al. (2020) (9)	Bhatraju et al. (2020) (7)	Cozzi et al. (2020) (12)	Gatti (2020) (15)	Guan et al. (2020) (5)	Ippolito et al. (2020) (13)
	n= 21	n= 2	n= 23	N = 234	N = 260	n= 274	n= 468
Chest X-ray on admission (days from symptom onset)	Mean: 3.5 days	2 days	Mean (SD): 7±4 days	Range: 2-15 days	Not reported	Median: 4 days	More than 5 days in 57.7% of patients
Abnormal N %	20 (95)	1 (50%)	23 (100)	223 (94.4)	159 (61.5)	162 (59)	
Findings							
Bilateral Pneumonia	11(52)		23 (100)	162 (69.2)	99 (38)	100 (36.5)	301 (64.5)
Unilateral Pneumonia							
Type of Infiltrate							
Interstitial involvement		1 (50)		147 (62.8)		12 (4.4)	335 (71.1)

Airspace								279 (60.5)
Reticulo-nodular infiltrates	11 (52)			135 (57.7)				
Ground-glass opacity	10 (48)						55 (20.4)	
Consolidation	4 (19)			137 (58.5)				245(52.5)
Location				31 (13.1)				
Lower				99 (41)	147 (56)			335(71.7)
Mid					110 (42)			290(62.1)
Upper					37(14)			
Diffuse				135 (57.7)				
Centrality								
Peripheral					69 (26)			292(62.5)
Central	5 (23.8)			39 (16.7)	34 (13)			
Other								
Pleural effusion			**0**		17 (6)			
				67.1%				

(cont.)

	Lomoro (2020) (17)	Ng et al. (2020) (8)	Pakray. (2020) (18)	Rodriguez-Morales et al. (2020) (3)	Rodriguez-Morales et al. (2020) (3)	Stephanie et al. (2020) (16)	Weinstock al. (2020) (11)	Wong et al. (2020) (4)	Yoon et al. (2020) (10)
	n= 58 32 with x-ray	n= 5	n= 173 with 186 abnormal x-ray *	N=620	n= 126	N = 508 254-SARS Cov2+	n= 636	n= 64	n= 9
Chest X-ray on admission (days from symptom onset)	Not reported	Median (range): 3 (1-7) days	Not reported	Not reported	Not reported	32% ≤2 days 24% 3-6 days 23% 7-11 days 22% >11 days.	Not reported	Not reported	Not reported
Abnormal N %	27 (77.1)	3 (60)	148(86)				265 (41.7)	44 (69)	3 (33.3)

Findings								
Bilateral Pneumonia	25 (78.1)		165(88.7*)	72.9%	50 (39.7)		133 (20.9)	32 (63)
Unilateral Pneumonia	2 (6.2)		21(11.3*)	25%	13 (10.3)			19 (37)
Type of Infiltrate							151 (23.7)	
Interstitial involvement			59(31.7*)			127 (51)	120 (18.9)	
Airspace			53(28.4*)					
Reticulo-nodular infiltrates							34 (5.3)	
Ground-glass opacity	12 (37.5)			68.5%	58 (46)			21(59%)
Consolidation	15 (46.9)	3(60)				7 (3)	215 (33.8)	30 (59)
Location							128 (20.1)	
Lower	15 (46.9)	75(40.3*)				84 (34)	6 (0.9)	32(63)
Mid								0
Upper	1(3.1)					7 (3)		
Diffuse		99(53.2*)				106 (43)	225 (35.4)	19(37)
Centrality							45 (7.1)	
Peripheral						52 (21)		26 (51)
Central							2 (0.3)	6 (12)
Other								
Pleural effusion	0							2(3)

Appendix 2. Studies that described Diagnostic Accuracy of Chest Radiography compared to RT-PCR

Study/year/ Country	Study Design/ Inclusive Dates	Population N (n= RTPCR+)	Chest X-ray Timing from Symptom onset Definition / Criteria of Positive Index Test	Results			Risk of Bias
				Sensitivity (95% CI)	Specificity (95% CI)	Other findings	
Borakati et al. (2020) (20) London, UK	Cross-sectional March 16-April 16, 2020	1198 (763) General population seen in the ED	Not mentioned British Society of Thoracic Imaging reporting templates.	56 (51 to 60)	60 (0.54 to 0.65)	When CXR report is considered as an ordered scale, worsening grades were associated more strongly with RT-PCR positivity, with a 1.94x increase in odds for each grade.	Unclear
Choudhury et al (2020) (21) India	Retrospective cohort Period of 6 weeks (unspecified)	97 (29) Symptomatic patients seen in the respiratory unit	Mean of 5.56 days (1-10 days) Unvalidated Likert score based on a format for reporting Chest CT scan features of	75.86 (56.5–90)			Low

			COVID-19 Simpson et al.				
Cozzi et al. (2020) (12) Milan Italy	Retrospective cohort February 24th to April 8th 2020	535 (408)	Not mentioned Presence of interstitial infiltrates – associated or not with alveolar infiltrates – with predominantly bilateral and basal distribution	89 (85.5-91.8)	60.6 51.6-69.2	Overall high sensitivity (89%)with higher specificity (66%) for more experienced radiologists.	Unclear
Gatti, 2020 (15) Italy	Cross sectional March 1 – March 31, 2020	260 (260)	Not mentioned Unclear	61.1 (55–67	Not calculable	Dyspnea (p = 0.004) and a longer interval (> 4 days) between the onset of symptoms and the execution of CXR (p = 0.0002) were typical of CXR+	Low
Hwang et al (2020) (14) Korea	Retrospective cohort Jan 31 – March 10, 2021	332 (16)	Median of 5 day (IQR 9) Any abnormality on Chest x-ray suggesting pneumonia	68.8 (41-89)	66.7 (61-72)	Diagnostic performance of Chest x-ray did not show significant difference between patients with and without symptoms of acute respiratory disease Chest x-ray exhibited higher specificity (67.0% vs. 49.0%; p = 0.020) in patients with symptom duration of ≤ 3 days while it had higher PPV in patients with symptoms > 3 days (3.3% vs 19.5% p – 0.016)	Unclear
Ippolito et al. (2020) (13)	Cross-sectional March 1-13, 2020	518(204)	Not mentioned Presence of parenchymal	57 95-64	89 85-92	Sensitivity was higher for patients	Unclear

Lombardy Italy			abnormalities such as alveolar and interstitial opacities, consolidation, pleural effusion			with symptom onset > 5 days compared to ≤ 5 days (76 % [62–87] vs 37 % [24–52]) and in patients > 50 years old compared to ≤ 50 years (59 % [48–69] vs 47 % [23–72]), at the expense of a slightly lower specificity (68 % [45–86] and 82 % [73–89], respectively).	
Murphy et al (2020) (22) Netherlands	Retrospective cohort March 4-April 6, 2020	454 (223)	Not mentioned Category 3: lung opacity consistent with COVID-19	65 (59-72)	81 (75-85)	Performance of artificial intelligence system in the detection of coronavirus disease 2019 on chest radiographs was comparable with that of six independent readers	Low
Pare et al. (2020) (23) Boston, USA	Retrospective cohort March 20 and April 6, 2020	43(27)	Not mentioned Opacity, consolidation, or airspace disease	56.3 (33.2 - 76.9)	75.5 (50 - 90.3)		High
Stephanie et al (2020) (16) USA	Retrospective Cohort Academic medical center, tertiary hospital, community center	508 (254)	Median time 4 days. Individual rating by radiologists regarding likelihood of COVID 19 based on chest x ray finding	58% (0.58-0.62)	83%	CXR sensitivity in COVID-19 detection increases with time Mild severity or minor findings on CXRs were the main determinants of false negative result	Low

Stevens et al. (2020) (19) UK	Cross sectional March 17 – April 30 2020.	320 (248)	Not mentioned British Society of Thoracic Imaging reporting templates	94.4 (91-97)	88.9 (79-95)		High

Appendix 3. GRADE Evidence Profile

Question: Should chest radiography be used to diagnose COVID-19 in patients with suspected COVID-19?

Sensitivity	0.74 (95% CI: 0.59 to 0.85)
Specificity	0.76 (95% CI: 0.67 to 0.83)

Prevalences	0.5%	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 of 0.5%	pre-test probability of 1%	pre-test probability of 5%	
True positives (patients with COVID-19)	9 studies 3659 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	serious [c]	none	4 (3 to 4)	7 (6 to 9)	37 (30 to 43)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having COVID-19)								1 (1 to 2)	3 (1 to 4)	13 (7 to 20)	
True negatives (patients without COVID-19)	9 studies 3659 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	serious [c]	none	756 (667 to 826)	752 (663 to 822)	722 (637 to 789)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having COVID-19)								239 (169 to 328)	238 (168 to 327)	228 (161 to 313)	

Explanations

a. more than 50% of the studies had unclear to high risk of bias in the domains of Patient Selection, Index Test, Reference Standard, and Flow and Timing based on QUADAS-2

b. I2 > 50%; variable timing and definition of positive test, issues with intrarater and interrater reliability
c. wide confidence intervals, sample size

Appendix 4. Forest Plots

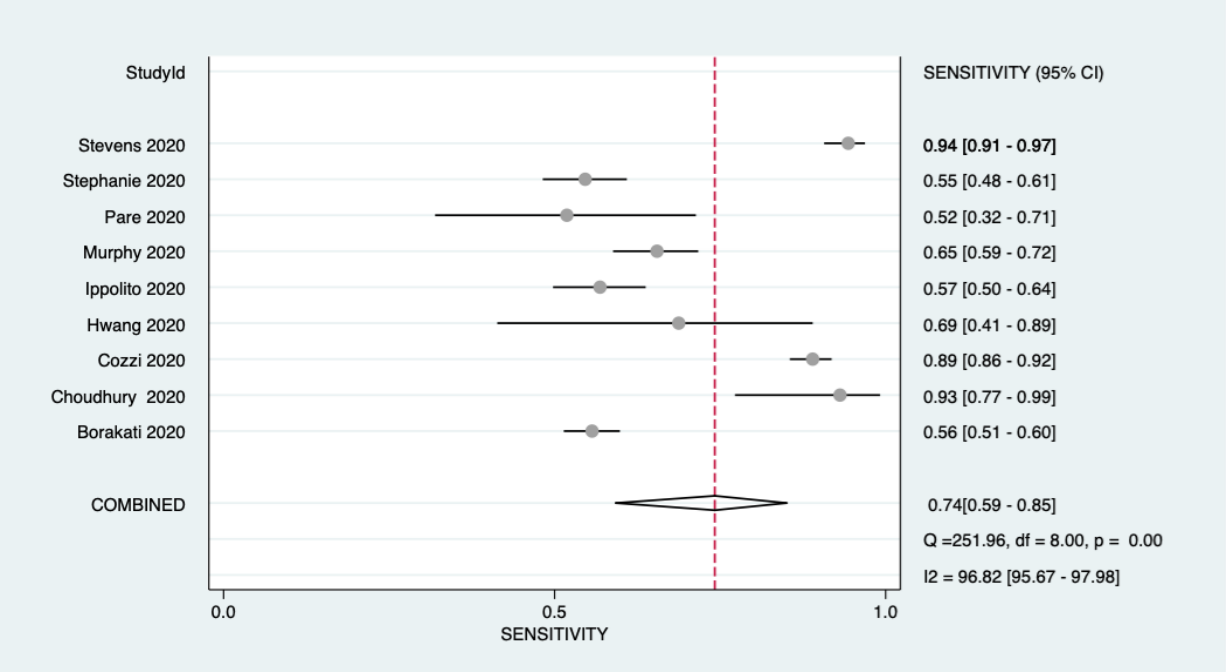


Figure 2. Forest plot showing the sensitivity of CXR diagnosing COVID-19

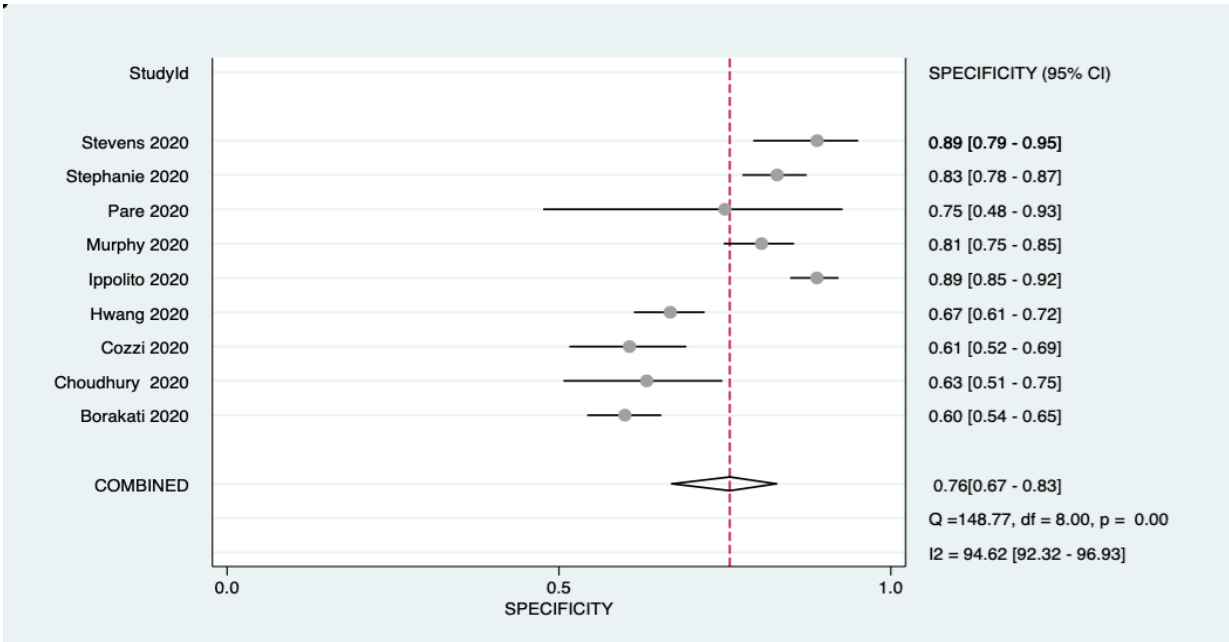
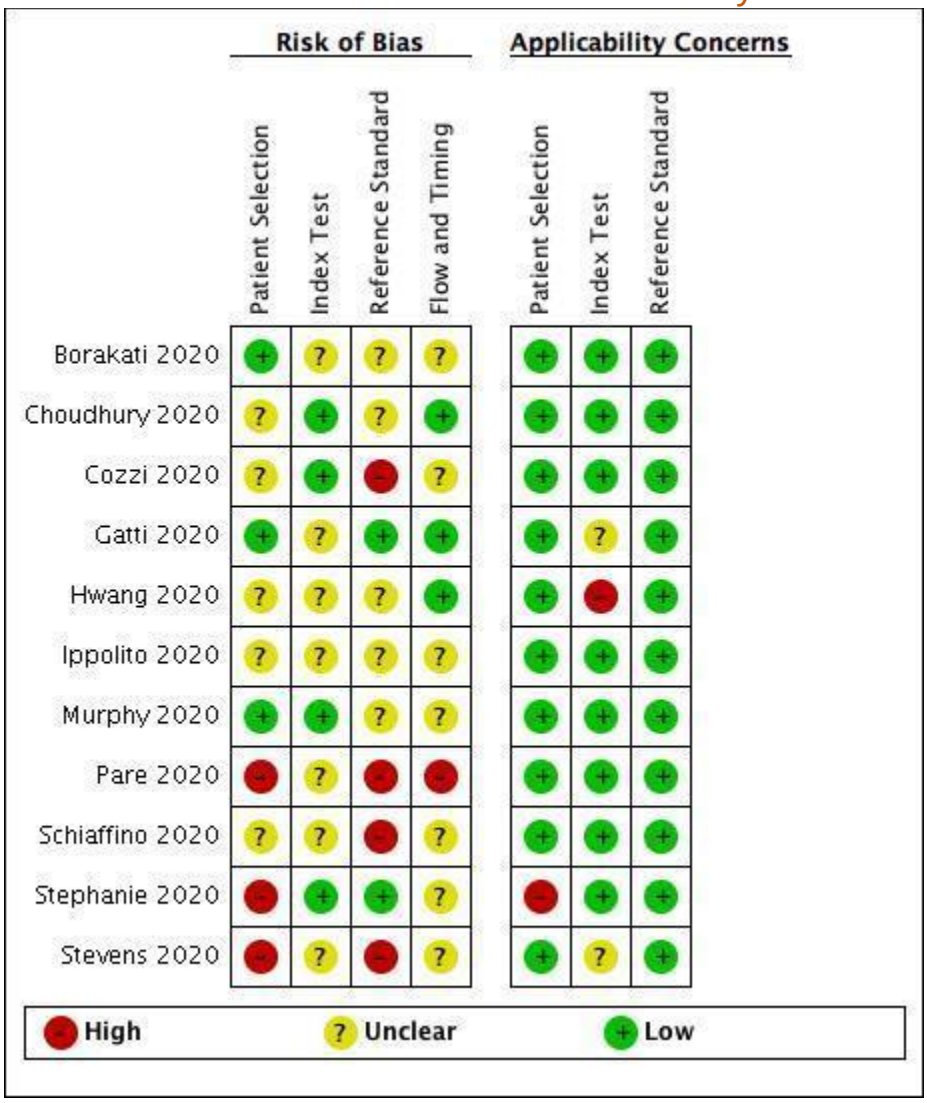


Figure 3. Forest plot showing the specificity of CXR diagnosing COVID-19

Appendix 5. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study



Appendix 6. Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies