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Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 (Review)

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[Diagnostic Test Accuracy Review]

Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19

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ABSTRACT

Background

COVID-19 illness is highly variable, ranging from infection with no symptoms through to pneumonia and life-threatening consequences. Symptoms such as fever, cough, or loss of sense of smell (anosmia) or taste (ageusia), can help flag early on if the disease is present. Such information could be used either to rule out COVID-19 disease, or to identify people who need to go for COVID-19 diagnostic tests. This is the second update of this review, which was first published in 2020.

Objectives

To assess the diagnostic accuracy of signs and symptoms to determine if a person presenting in primary care or to hospital outpatient settings, such as the emergency department or dedicated COVID-19 clinics, has COVID-19.

Search methods

We undertook electronic searches up to 10 June 2021 in the University of Bern living search database. In addition, we checked repositories of COVID-19 publications. We used artificial intelligence text analysis to conduct an initial classification of documents. We did not apply any language restrictions.

Selection criteria

Studies were eligible if they included people with clinically suspected COVID-19, or recruited known cases with COVID-19 and also controls without COVID-19 from a single-gate cohort. Studies were eligible when they recruited people presenting to primary care or hospital

outpatient settings. Studies that included people who contracted SARS-CoV-2 infection while admitted to hospital were not eligible. The minimum eligible sample size of studies was 10 participants. All signs and symptoms were eligible for this review, including individual signs and symptoms or combinations. We accepted a range of reference standards.

Data collection and analysis

Pairs of review authors independently selected all studies, at both title and abstract, and full-text stage. They resolved any disagreements by discussion with a third review author. Two review authors independently extracted data and assessed risk of bias using the QUADAS-2 checklist, and resolved disagreements by discussion with a third review author. Analyses were restricted to prospective studies only. We presented sensitivity and specificity in paired forest plots, in receiver operating characteristic (ROC) space and in dumbbell plots. We estimated summary parameters using a bivariate random-effects meta-analysis whenever five or more primary prospective studies were available, and whenever heterogeneity across studies was deemed acceptable.

Main results

We identified 90 studies; for this update we focused on the results of 42 prospective studies with 52,608 participants. Prevalence of COVID-19 disease varied from 3.7% to 60.6% with a median of 27.4%. Thirty-five studies were set in emergency departments or outpatient test centres (46,878 participants), three in primary care settings (1230 participants), two in a mixed population of in- and outpatients in a paediatric hospital setting (493 participants), and two overlapping studies in nursing homes (4007 participants). The studies did not clearly distinguish mild COVID-19 disease from COVID-19 pneumonia, so we present the results for both conditions together.

Twelve studies had a high risk of bias for selection of participants because they used a high level of preselection to decide whether reverse transcription polymerase chain reaction (RT-PCR) testing was needed, or because they enrolled a non-consecutive sample, or because they excluded individuals while they were part of the study base. We rated 36 of the 42 studies as high risk of bias for the index tests because there was little or no detail on how, by whom and when, the symptoms were measured. For most studies, eligibility for testing was dependent on the local case definition and testing criteria that were in effect at the time of the study, meaning most people who were included in studies had already been referred to health services based on the symptoms that we are evaluating in this review.

The applicability of the results of this review iteration improved in comparison with the previous reviews. This version has more studies of people presenting to ambulatory settings, which is where the majority of assessments for COVID-19 take place. Only three studies presented any data on children separately, and only one focused specifically on older adults.

We found data on 96 symptoms or combinations of signs and symptoms. Evidence on individual signs as diagnostic tests was rarely reported, so this review reports mainly on the diagnostic value of symptoms. Results were highly variable across studies. Most had very low sensitivity and high specificity. RT-PCR was the most often used reference standard (40/42 studies).

Only cough (11 studies) had a summary sensitivity above 50% (62.4%, 95% CI 50.6% to 72.9%)); its specificity was low (45.4%, 95% CI 33.5% to 57.9%)). Presence of fever had a sensitivity of 37.6% (95% CI 23.4% to 54.3%) and a specificity of 75.2% (95% CI 56.3% to 87.8%). The summary positive likelihood ratio of cough was 1.14 (95% CI 1.04 to 1.25) and that of fever 1.52 (95% CI 1.10 to 2.10). Sore throat had a summary positive likelihood ratio of 0.814 (95% CI 0.714 to 0.929), which means that its presence increases the probability of having an infectious disease other than COVID-19.

Dyspnoea (12 studies) and fatigue (8 studies) had a sensitivity of 23.3% (95% CI 16.4% to 31.9%) and 40.2% (95% CI 19.4% to 65.1%) respectively. Their specificity was 75.7% (95% CI 65.2% to 83.9%) and 73.6% (95% CI 48.4% to 89.3%). The summary positive likelihood ratio of dyspnoea was 0.96 (95% CI 0.83 to 1.11) and that of fatigue 1.52 (95% CI 1.21 to 1.91), which means that the presence of fatigue slightly increases the probability of having COVID-19.

Anosmia alone (7 studies), ageusia alone (5 studies), and anosmia or ageusia (6 studies) had summary sensitivities below 50% but summary specificities over 90%. Anosmia had a summary sensitivity of 26.4% (95% CI 13.8% to 44.6%) and a specificity of 94.2% (95% CI 90.6% to 96.5%). Ageusia had a summary sensitivity of 23.2% (95% CI 10.6% to 43.3%) and a specificity of 92.6% (95% CI 83.1% to 97.0%). Anosmia or ageusia had a summary sensitivity of 39.2% (95% CI 26.5% to 53.6%) and a specificity of 92.1% (95% CI 84.5% to 96.2%). The summary positive likelihood ratios of anosmia alone and anosmia or ageusia were 4.55 (95% CI 3.46 to 5.97) and 4.99 (95% CI 3.22 to 7.75) respectively, which is just below our arbitrary definition of a 'red flag', that is, a positive likelihood ratio of at least 5. The summary positive likelihood ratio of ageusia alone was 3.14 (95% CI 1.79 to 5.51).

Twenty-four studies assessed combinations of different signs and symptoms, mostly combining olfactory symptoms. By combining symptoms with other information such as contact or travel history, age, gender, and a local recent case detection rate, some multivariable prediction scores reached a sensitivity as high as 90%.

Authors' conclusions

Most individual symptoms included in this review have poor diagnostic accuracy. Neither absence nor presence of symptoms are accurate enough to rule in or rule out the disease. The presence of anosmia or ageusia may be useful as a red flag for the presence of COVID-19. The presence of cough also supports further testing. There is currently no evidence to support further testing with PCR in any individuals presenting only with upper respiratory symptoms such as sore throat, coryza or rhinorrhoea.

Combinations of symptoms with other readily available information such as contact or travel history, or the local recent case detection rate may prove more useful and should be further investigated in an unselected population presenting to primary care or hospital outpatient settings.

The diagnostic accuracy of symptoms for COVID-19 is moderate to low and any testing strategy using symptoms as selection mechanism will result in both large numbers of missed cases and large numbers of people requiring testing. Which one of these is minimised, is determined by the goal of COVID-19 testing strategies, that is, controlling the epidemic by isolating every possible case versus identifying those with clinically important disease so that they can be monitored or treated to optimise their prognosis. The former will require a testing strategy that uses very few symptoms as entry criterion for testing, the latter could focus on more specific symptoms such as fever and anosmia.

PLAIN LANGUAGE SUMMARY

How accurate are symptoms and medical examination to diagnose COVID-19?

Key messages

- The results suggest that a single symptom included in this review cannot accurately diagnose COVID-19.

- Loss of sense of taste or smell could be a 'red flag' for the presence of COVID-19. Cough or fever might be useful to identify people who might have COVID-19. These symptoms might be useful to prompt further testing when they are present.

- We need more research to investigate combinations of symptoms and signs with other information such as recent contact or travel history, or vaccination status, and in children, and adults aged 65 years and over.

What are symptoms or signs of COVID-19?

Symptoms are experienced by patients. COVID-19 symptoms include cough, sore throat, high temperature, diarrhoea, headache, muscle or joint pain, fatigue, and loss of sense of smell and taste.

Signs are measured by healthcare workers during clinical examination. They include lung sounds, blood pressure, blood oxygen level and heart rate.

Symptoms and signs of COVID-19 might be important to help people know whether they and the people they come into contact with should isolate at home, undergo testing with a rapid lateral flow test or PCR (laboratory-based) test, or be hospitalised.

What did we want to find out?

Symptoms and signs of COVID-19 are varied and may indicate other diseases, not just COVID-19. We wanted to know how accurate diagnosis of COVID-19 is, based on symptoms and signs from medical examination. We were interested in people with suspected COVID-19, who go to their doctor, outpatient test centres or hospital.

What did we do?

We searched for studies that assessed the accuracy of symptoms and signs to diagnose COVID-19. Studies had to be conducted in general practice, outpatient test centres or hospital outpatient settings only. We only included studies of people in hospital if signs and symptoms were recorded when they were admitted to the hospital, for example through the emergency department.

What did we find?

We focused on 42 studies with 52,608 participants in this review. The studies assessed 96 separate or combined symptoms and signs. Thirty-five studies were conducted in emergency departments or outpatient COVID-19 test centres (46,878 participants), 3 studies in general practice (1230 participants), 2 studies in children's hospitals (493 in- and outpatients), and 2 studies in nursing homes (4007 participants). The studies were conducted in 18 different countries around the world. Twenty-three studies were conducted in Europe, 8 in North-America, 5 in Asia, and 3 in South-America and 3 in Australia. We didn't find any studies conducted in Africa. Three focused specifically on children, and only 1 focused on adults aged 65 years and over.

Most studies did not clearly distinguish between mild and severe COVID-19, so we present the results for mild, moderate and severe disease together.

Few studies reported individual signs as diagnostic tests, so we focus mainly on the diagnostic value of symptoms. The most frequently reported symptoms were cough, fever, shortness of breath and sore throat.

According to the studies in our review, in a group of 1000 people with suspected COVID-19 of whom 270 (27%) would actually have COVID-19, around 567 people would have a cough. Of these 567, 168 would actually have COVID-19. Of the 433 who do not have a cough, 102 would have COVID-19. In the same 1000 people, around 283 people would have a fever. Of these 283, 102 would actually have COVID-19. Of the 717 people without fever, 168 would have COVID-19.

Someone who has lost their sense of smell or taste is five times more likely to have COVID-19 than someone who hasn't.

Other symptoms, such as a sore throat or runny nose, are more likely to indicate the presence of an infectious disease other than COVID-19. In the same 1000 people as described above, around 362 people would have a sore throat. Of these, only 84 would actually have COVID-19. Of the 638 patients without sore throat, 186 would have COVID-19. We found similar figures for having a runny nose.

What are the limitations of the evidence?

The results of this updated review are more reliable than those in previous versions as we included more high-quality studies. However, the accuracy of individual symptoms varied across studies and the diagnostic value of symptoms such as fever, cough or other respiratory symptoms might still be overestimated, as most studies deliberately included participants because they had these symptoms.

The results do not clearly differentiate between people with mild, moderate or severe COVID-19. Only a few studies investigated the symptom-based diagnosis of COVID-19 in children or older adults.

How up to date is this review?

This review updates our previous review. The evidence is up to date to June 2021.

SUMMARY OF FINDINGS

Summary of findings 1. Symptoms to determine if a patient presenting in primary care or hospital outpatient setting has COVID-19

Symptoms to determine if a patient presenting in primary care or hospital outpatient setting has COVID-19

Patient or population: people with COVID-19 symptoms

Setting: primary care or hospital outpatient departments

Index test(s): symptoms of COVID-19

Target condition: SARS-CoV-2 infection (symptomatic of any severity); mild or moderate COVID-19; severe or critical COVID-19

Reference standard: RT-PCR

Top 10 of most reported symptoms to determine if a patient presenting in primary care or hospital outpatient setting has COVID-19 (prospective cross-sectional studies only). We estimated pooled sensitivity and specificity only for prospective studies with a low risk of bias rating for participant selection.

Symptom	Setting	Number of studies/number of participants	Sensitivity (ranges)	Specificity (ranges)	Strength of evidence Number of studies with high risk of bias per QUADAS-2 domain: participant selection/index test/ reference standard/flow and timing
Cough	Primary care	2/414	70% to 80%	16% to 30%	2/1/0/0
	Outpatient clinics/ED	25/32,756	14% to 86%	15% to 88%	7/20/1/1
	Mixed: paediatric hospital inpatients/ outpatients	2/493	40% to 47%	29% to 61%	0/2/0/0
	Nursing homes	1/3764	63%	38%	0/1/0/0
	All settings (only prospective studies with low risk of bias for participant selection)	**11/18,702**	**Summary estimate:** **62% (95% CI 51% to 73%)**	**Summary estimate:** **45% (95% CI 34% to 58%)**	

Fever	Primary care	1/334	33%	73%	1/1/0/0
	Outpatient clinics/ED	25/40,278	6% to 78%	8% to 99%	6/21/1/1
	Mixed: paediatric hospital inpatients/ outpatients	2/493	47% to 51%	30% to 53%	0/2/0/0
	Nursing homes	1/3771	63%	58%	0/1/0/0
	All settings (only prospective studies with low risk of bias for participant selection)	**12/28,495**	**Summary estimate:** **38% (95% CI 23% to 54%)**	**Summary estimate:** **75% (95% CI 56% to 88%)**	
Dyspnoea	Primary care	1/334	15%	82%	1/1/0/0
	Outpatient clinics/ED	24/30,809	6% to 77%	31% to 95%	7/21/1/1
	Mixed: paediatric hospital inpatients/ outpatients	2/493	7% to 16%	86% to 92%	0/2/0/0
	Nursing homes	1/3622	30%	61%	0/1/0/0
	All settings (only prospective studies with low risk of bias for participant selection)	**12/19,545**	**Summary estimate:** **23% (95% CI 16% to 32%)**	**Summary estimate:** **76% (95% CI 65% to 84%)**	
Sore throat	Primary care	2/414	19% to 80%	61% to 88%	2/1/0/0
	Outpatient clinics/ED	21/26,470	3% to 77%	21% to 94%	8/19/1/1
	Mixed: paediatric hospital inpatients/ outpatients	2/493	0% to 35%	79% to 89%	0/2/0/0
	Nursing homes	1/2675	10%	86%	0/1/0/0
	All settings (only prospective studies with low risk of bias for participant selection)	**10/14,548**	**Summary estimate:** **31% (95% CI 20% to 45%)**	**Summary estimate:** **62% (95% CI 47% to 75%)**	
Headache	Primary care	2/414	11% to 40%	71% to 85%	2/1/0/0
	Outpatient clinics/ED	19/26,135	2% to 93%	9% to 93%	10/16/1/1
	Mixed: paediatric hospital inpatients/ outpatients	2/493	0% to 27%	76% to 95%	0/2/0/0

	Nursing homes	-	-	-	-
	All settings (only prospective studies with low risk of bias for participant selection)	**7/10899**	**Summary estimate:** **36% (95% CI 17% to 60%)**	**Summary estimate:** **73% (95% CI 53% to 86%)**	
Diarrhoea	Primary care	1/334	4%	93%	1/1/0/0
	Outpatient clinics/ED	19/24042	10% to 64%	44% to 95%	6/17/1/1
	Mixed: paediatric hospital inpatients/ outpatients	2/493	6% to 20%	90% to 93%	0/2/0/0
	Nursing homes	1/1286	18%	84%	0/1/0/0
	All settings (only prospective studies with low risk of bias for participant selection)	**11/13,669**	**Summary estimate:** **19% (95% CI 16% to 22%)**	**Summary estimate:** **84% (95% CI 79% to 88%)**	
Myalgia	Primary care	1/334	26%	81%	1/1/0/0
	Outpatient clinics/ED	17/16,106	20% to 84%	22% to 92%	9/15/0/0
	Mixed: paediatric hospital inpatients/ outpatients	1/319	0%	92%	0/1/0/0
	Nursing homes	-	-	-	-
	All settings (only prospective studies with low risk of bias for participant selection)	**6/2684**	**Summary estimate:** **38% (95% CI 21% to 58%)**	**Summary estimate:** **75% (95% CI 58% to 87%)**	
Anosmia	Primary care	2/1150	26% to 41%	88% to 93%	1/2/0/0
	Outpatient clinics/ED	18/18,958	1% to 65%	70% to 99%	9/15/1/2
	Mixed: paediatric hospital inpatients/ outpatients	-	-	-	-
	Nursing homes	-	-	-	-
	All settings	**7/9456**	**Summary estimate:**	**Summary estimate:**	

	(only prospective studies with low risk of bias for participant selection)		**26% (95% CI 14% to 45%)**	**94% (95% CI 91% to 97%)**	
Fatigue	Primary care	1/334	19%	71%	1/1/0/0
	Outpatient clinics/ED	15/12,369	15% to 90%	18% to 94%	6/14//1/1
	Mixed: paediatric hospital inpatients/ outpatients	2/493	0% to 4%	95% to 97%	0/2/0/0
	Nursing homes	1/1286	22%	87%	0/1/0/0
	All settings (only prospective studies with low risk of bias for participant selection)	**8/7967**	**Summary estimate:** **40% (95% CI 19% to 65%)**	**Summary estimate:** **74% (95% CI 48% to 89%)**	
Chills/shivers	Primary care	2/414	19% to 20%	89% to 93%	2/1/0/0
	Outpatient clinics/ED	10/21,980	26% to 81%	28% to 97%	4/10/0/0
	Mixed: paediatric hospital inpatients/ outpatients	1/174	8%	98%	0/1/0/0
	Nursing homes	-	-	-	-
	All settings (only prospective studies with low risk of bias for participant selection)	**5/14,472**	**Summary estimate:** **25% (95% CI 15% to 39%)**	**Summary estimate:** **85% (95% CI 72% to 93%)**	

CI: confidence interval; **ED:** emergency department; **RT-PCR:** reverse transcription polymerase chain reaction

BACKGROUND

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus and resulting COVID-19 pandemic present important diagnostic evaluation challenges. These range from, on the one hand, understanding the value of signs and symptoms in predicting possible infection, assessing whether existing biochemical and imaging tests can identify infection and recognise patients needing critical care, and on the other hand, evaluating whether new diagnostic tests can allow accurate rapid and point-of-care testing. Also, the diagnostic aims are diverse, including identifying current infection, ruling out infection, identifying people in need of care escalation, or testing for past infection and immunity.

This review is the second update of a review summarising evidence of the diagnostic accuracy of presenting clinical signs and symptoms for COVID-19. This review is part of a suite of reviews on the diagnosis of SARS-CoV-2 infection and COVID-19 disease, exploring the accuracy of antibody tests (Deeks 2020a), routine laboratory testing (Stegeman 2020), rapid point-of-care tests (Dinnes 2021) and thoracic imaging tests (Islam 2021).

Target condition being diagnosed

The key target conditions for this suite of reviews are current SARS-CoV-2 infection, current COVID-19, and past SARS-CoV-2 infection.

For current infection, the severity of the disease is of importance. SARS-CoV-2 infection can be asymptomatic (no symptoms); mild or moderate (symptoms such as fever, cough, loss of smell (anosmia) or taste (ageusia), aches, lethargy but without difficulty breathing at rest); severe (symptoms with breathlessness and increased respiratory rate indicative of pneumonia and oxygen need); or critical (requiring intensive support due to severe acute respiratory syndrome (SARS) or acute respiratory distress syndrome (ARDS), shock or other organ dysfunction (NIH 2021). People with COVID-19 pneumonia (severe or critical disease) require different patient management, which makes it important to distinguish between them and mild or moderate disease.

Thus, there are three target conditions for current infection:

1. SARS-CoV-2 infection (asymptomatic or symptomatic of any severity);
2. mild or moderate COVID-19 disease;
3. COVID-19 pneumonia (severe or critical).

Here we summarise the evidence on signs and symptoms; as a result asymptomatic SARS-CoV-2 and past SARS-CoV-2 infection are out of scope for this review.

Index test(s)

Signs and symptoms

Signs and symptoms are used in the initial diagnosis of suspected COVID-19 disease, and to identify people with COVID-19 pneumonia. Symptoms are what are experienced by patients, for example cough or nausea. Signs are obtained by clinical examination. Signs of COVID-19 examined in this review include lung sounds, blood pressure, blood oxygen level and heart rate.

Key symptoms that have been associated with mild to moderate COVID-19 disease include: troublesome dry cough (for example, coughing more than usual over a one-hour period, or three or more coughing episodes in 24 hours), fever at examination greater than 37.8 °C, diarrhoea, headache, breathlessness on light exertion, muscle pain, fatigue, and loss of sense of smell and taste (Struyf 2021). Signs and symptoms indicating possible pneumonia (severe or critical disease) include breathlessness at rest, loss of appetite, confusion, pain or pressure in the chest, and temperature above 38 °C.

Clinical pathway

Important in the context of COVID-19 is that the pathway is multifaceted because it is designed to care for the diseased individual and to protect the community from further spread. Decisions about patient and isolation pathways for COVID-19 vary according to health services and settings, available resources, and stages of the epidemic. They will change over time if and when effective treatments are identified and populations are increasingly vaccinated. The decision points between these pathways vary, but all include points at which knowledge of the accuracy of diagnostic information is needed to inform rational decision making.

Prior test(s)

Prior testing will depend on whether people are being investigated for SARS-CoV-2 infection, mild COVID-19 or COVID-19 pneumonia. In this review on signs and symptoms, no prior tests are required because signs and symptoms are used in the initial diagnosis of suspected SARS-CoV-2 infection, and in identifying people with mild COVID-19 or COVID-19 pneumonia.

Role of index test(s)

Signs and symptoms are used as triage tests, that is, to rule out SARS-CoV-2 infection or COVID-19 disease, but also to identify people with possible COVID-19 who may require further testing, care escalation or isolation.

Alternative test(s)

We are producing a suite of Cochrane 'living systematic reviews', which will summarise evidence on the clinical accuracy of different tests and diagnostic features, grouped according to the present research questions and settings in the diagnosis of SARS-CoV-2 infection and COVID-19. Summary estimates of accuracy from these reviews will help inform diagnostic, screening, isolation, and patient-management decisions.

New tests are being developed and evidence is emerging at an unprecedented rate during the COVID-19 pandemic. We will aim to update these reviews as often as is feasible to ensure that they provide the most up-to-date evidence about test accuracy.

These reviews are being produced rapidly to assist in providing a central resource of evidence to assist in the COVID-19 pandemic, summarising available evidence on the accuracy of the tests and presenting characteristics.

Other Cochrane diagnostic test accuracy (DTA) reviews in the suite of reviews are addressing the following tests.

- Chest imaging (computed tomography (CT), chest X-ray and ultrasound (Islam 2021)
- Routine laboratory testing, such as for C-reactive protein (CRP) and procalcitonin (PCT) (Stegeman 2020)

- Antibody tests (Deeks 2020a)
- Laboratory-independent point-of-care and near-patient molecular and antigen tests (Dinnes 2021)
- Molecular laboratory tests (in preparation)

Rationale

It is essential to understand the accuracy of diagnostic features and tests to identify the best way they can be used in different settings to develop effective diagnostic and management pathways. For example, the absence of a highly sensitive sign or symptom is good for ruling out COVID-19, while the presence of a sign or symptom with high specificity is good for ruling in COVID-19 ('red flag').

OBJECTIVES

To assess the diagnostic accuracy of signs and symptoms to determine if a person presenting in primary care or to hospital outpatient settings, such as the emergency department or dedicated COVID-19 clinics, has COVID-19.

Secondary objectives

Where data are available, we investigated diagnostic accuracy (either by stratified analysis or meta-regression) according to:

- days since symptom onset;
- population (children, adults, older adults ≥ 65 years);
- reference standard;
- study design;
- setting; and
- risk of bias in participant selection (as scored using QUADAS-2)

Objectives of future updates of this review

This review will no longer be updated in its current form. Objectives of any future updates of this review are:

- to look at a broader approach involving a combination of signs and symptoms with other easy-to-obtain information, for example, point-of-care test results;
- to perform the listed stratified analyses;
- to explore seasonality;
- to investigate people who require respiratory support or intensive care.

Summary of previous review

In the first update of our review, we found 44 relevant studies with 26,884 participants. Prevalence of COVID-19 disease varied from 3% to 71% with a median of 21%. There were three studies from primary care settings (1824 participants), nine studies from outpatient testing centres (10,717 participants), 12 studies performed in hospital outpatient wards (5061 participants), seven studies in hospitalised patients (1048 participants), 10 studies in the emergency department (3173 participants), and three studies in which the setting was not specified (5061 participants). The studies did not clearly distinguish mild COVID-19 disease from COVID-19 pneumonia, so we presented the results for both conditions together.

Fifteen studies had a high risk of bias for selection of participants because inclusion in the studies depended on the applicable testing and referral protocols, which included many of the signs and symptoms under study in the review. Five studies only included participants with pneumonia on imaging, suggesting that this is a highly selected population. In an additional 12 studies, we were unable to assess the risk for selection bias. This makes it very difficult to judge the validity of the diagnostic accuracy of the signs and symptoms from these included studies.

None of the studies presented any data on children separately, and only one focused specifically on older adults.

We found data on 84 signs and symptoms. Results were highly variable across studies. Most had very low sensitivity and high specificity. Only cough (25 studies) and fever (7 studies) had a summary sensitivity of at least 50% but specificities were moderate to low. Cough had a sensitivity of 67.4% (95% CI 59.8% to 74.1%) and specificity of 35.0% (95% CI 28.7% to 41.9%). Fever had a sensitivity of 53.8% (95% CI 35.0% to 71.7%) and a specificity 67.4% (95% CI 53.3% to 78.9%). The summary positive likelihood ratio of cough was only 1.04 (95% CI 0.97 to 1.11) and that of fever 1.65 (95% CI 1.41 to 1.93).

Anosmia alone (10 studies), ageusia alone (5 studies), and anosmia or ageusia (6 studies) had sensitivities below 50% but specificities over 85%. Anosmia had a summary sensitivity of 30.5% (95% CI 19.4% to 44.4%) and a specificity of 92.7% (95% CI 87.1% to 96.0%). Ageusia had a summary sensitivity of 29.4% (95% CI 15.1% to 49.5%) and a specificity of 89.0% (95% CI 77.6% to 94.9%). Anosmia or ageusia had a summary sensitivity of 41.0% (95% CI 27.0% to 56.6%) and a specificity of 90.5% (95% CI 81.2% to 95.4%). The summary positive likelihood ratios of anosmia alone and anosmia or ageusia were 4.16 (95% CI 3.10 to 5.60) and 4.31 (95% CI 3.00 to 6.18) respectively, which is just below our arbitrary definition of a red flag, that is, a positive likelihood ratio of at least 5. The summary positive likelihood ratio of ageusia alone was 2.67 (95% CI 1.96 to 3.64).

Only two studies assessed combinations of different signs and symptoms, mostly combining both fever and cough. These combinations had a specificity above 80%, but at the cost of very low sensitivity (< 30%).

We concluded that the majority of individual signs and symptoms included in the review appear to have very poor diagnostic accuracy, although this should be interpreted in the context of selection bias and heterogeneity between studies. Based on the available data, neither absence nor presence of signs or symptoms are accurate enough to rule in or rule out disease. The presence of anosmia or ageusia may be useful as a red flag for the presence of COVID-19. The presence of fever or cough may, given their high sensitivities, be useful as a triage tool for further testing.

New evidence since previous review

We found more studies on symptoms in people with suspected COVID-19 that used prospective data collection, allowing for more reliable estimation of measures of diagnostic accuracy. Moreover, this update contains new studies on the diagnostic value of 29 different combinations of signs and symptoms.

Limitations of previous review

The main weakness of the initial review and of the first update was the high risk of selection bias, with many studies including patients

who had already been admitted to hospital or who had presented to hospital settings with the intent to hospitalise.

The lack of data on combinations of signs and symptoms was an important evidence gap. Only two studies presented data on such combinations. The few composite signs and symptoms that were presented in those studies had little added diagnostic value compared to single tests.

METHODS

Criteria for considering studies for this review

Types of studies

We included published studies of all designs that produce estimates of sensitivity and specificity or provide data from which estimates can be computed. As of this update, we no longer included preprints. If no published version of previously included preprints could be found, we excluded these preprints.

As of this review update, we only included single-gate, cross-sectional designs (studies that recruit from a patient pathway before disease status has been ascertained). We included both studies that used retrospective data collection and studies that used prospective data collection, but the main findings of this review will be based on the prospective studies only, as retrospective studies tend to overestimate the diagnostic accuracy of the index tests (Rutjes 2006).

Studies had to have a minimum sample size of 10 participants.

Participants

Studies recruiting people presenting with a clinical suspicion of SARS-CoV-2 infection, based on a symptomatic presentation, were eligible. At least 50% of the study population had to present with COVID-19-compatible symptoms.

Index tests

- All signs and symptoms, including:
    - signs such as oxygen saturation, measured by oximetry and blood pressure;
    - symptoms, such as fever or cough.

Target conditions

To be eligible, studies had to identify at least one of:

- mild or moderate COVID-19;
- severe or critical COVID-19 (including COVID-19 pneumonia).

Asymptomatic infection with SARS-CoV-2 is out of scope for this review, considering it is by definition not possible to detect this based on signs and symptoms.

Reference standards

We anticipated that studies would use a range of reference standards. Although reverse transcription polymerase chain reaction (RT-PCR) is considered the best available test, due to rapidly evolving knowledge about the target conditions, multiple reference standards on their own as well as in combination have emerged.

We expected to encounter cases defined by:

- RT-PCR alone;
- RT-PCR, clinical expertise, and imaging (for example, CT thorax);
- repeated RT-PCR several days apart or from different samples;
- plaque reduction neutralisation test (PRNT) or enzyme-linked immunosorbent assay (ELISA) tests;
- information available at a subsequent time point;
- World Health Organization (WHO) and other case definitions (see Appendix 1).

This list is not exhaustive, and we recorded all reference standards encountered.

Search methods for identification of studies

The final search date for this version of the review is 10 June 2021.

Electronic searches

For this updated review, we used the University of Bern living search database as our primary register. This registry searches PubMed, Embase and preprint archives (medRxiv and bioRxiv) daily for COVID-19 research. The strategies to build the database can be found on the ISPM web site are described here ispmbern.github.io/COVID-19/ and in Appendix 2.

Due to the increased volume of literature a specific classifier was built for the review topic in Eppi reviewer. In brief, manual annotations of references on in- or exclusion from repeated retrieval dates from the previous versions of the review were partially used as training data and the remaining for validation and threshold for optimal recall determination. All references from the University of Bern living search database from 15 July 2020 till 10 June 2021 were run against the classifier and references labelled as potentially relevant were screened manually. See Appendix 3.

Searching other resources

We also checked our search results against two additional repositories of COVID-19 publications including:

- the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) 'COVID-19: Living map of the evidence' (eppi.ioe.ac.uk/COVID19_MAP/covid_map_v4.html);
- the Norwegian Institute of Public Health 'NIPH systematic and living map on COVID-19 evidence' (www.nornesk.no/forskningskart/NIPH_diagnosisMap.html).

Both of these repositories allow their contents to be filtered according to studies potentially relating to diagnosis, and both have agreed to provide us with updates of new diagnosis studies added. For this iteration of the review, we examined all diagnosis studies from both sources up to 10 June 2021.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Pairs of review authors independently screened studies. We resolved disagreements by discussion with a third, experienced review author for initial title and abstract screening, and

through discussion between three review authors for eligibility assessments.

Data extraction and management

Pairs of review authors independently performed data extraction. We resolved disagreements by discussion between three review authors.

We contacted study authors where we needed to clarify details or obtain missing information.

Assessment of methodological quality

Pairs of review authors independently assessed risk of bias and applicability concerns using the QUADAS-2 (Quality Assessment tool for Diagnostic Accuracy Studies) checklist, which was common to the suite of reviews but tailored to each particular review (Whiting 2011; Table 1). For this review, we excluded the questions on the nature of the samples as these were not relevant, and we added a question on who assessed the signs. We resolved disagreements by discussion between three review authors.

Statistical analysis and data synthesis

We presented results of estimated sensitivity and specificity using paired forest plots in Review Manager 2020, and tables as appropriate.

We considered tests to be useful in ruling out a serious infection in ambulatory care if their negative likelihood ratio (LR-) was lower than 0.20; conversely, we considered diagnostic tests useful as red flags for infections when their positive likelihood ratio (LR+) was 5.0 or higher (Jaeschke 1994; Van den Bruel 2010).

We disaggregated data by study design, reporting results from prospective studies separately from studies that used a retrospective design, which we assessed as prone to high risk of bias (Rutjes 2006). We focused on the results of prospective studies in this 2022 update. When interpreting the results, we made sure that the limitations of different study designs were carefully considered, using quality assessment and analysis.

We estimated summary sensitivity and specificity using a bivariate random-effects meta-analysis (Macaskill 2013). We undertook meta-analyses using the lme4 package (R 2020), implemented in MetaDTA (crsu.shinyapps.io/dta_ma/). We based the decision to pool data on the following criteria: clinically acceptable heterogeneity on visual inspection of the forest and ROC plots, the availability of at least five studies, and low risk of bias for participant selection.

Investigations of heterogeneity

Sources of heterogeneity that we investigated if adequate data were available are listed in the Secondary objectives, either using stratification (where we believed it was inappropriate to combine studies) or through meta-regression models.

In this version of the review, we have stratified by population (age group) and care setting.

Sensitivity analyses

We aimed to undertake sensitivity analyses considering the impact of unpublished studies, but this was not possible in this version of the review due to the small number of studies in each meta-analysis.

Assessment of reporting bias

We aimed to publish lists of studies that we know exist but for which we have not managed to locate reports, and request information to include in updates of these reviews. However, at the time of writing this version of the review, we are unaware of unpublished studies.

Summary of findings

We have listed our key findings in Summary of findings 1 to determine the strength of evidence for each test and findings, and to highlight important gaps in the evidence.

Updating

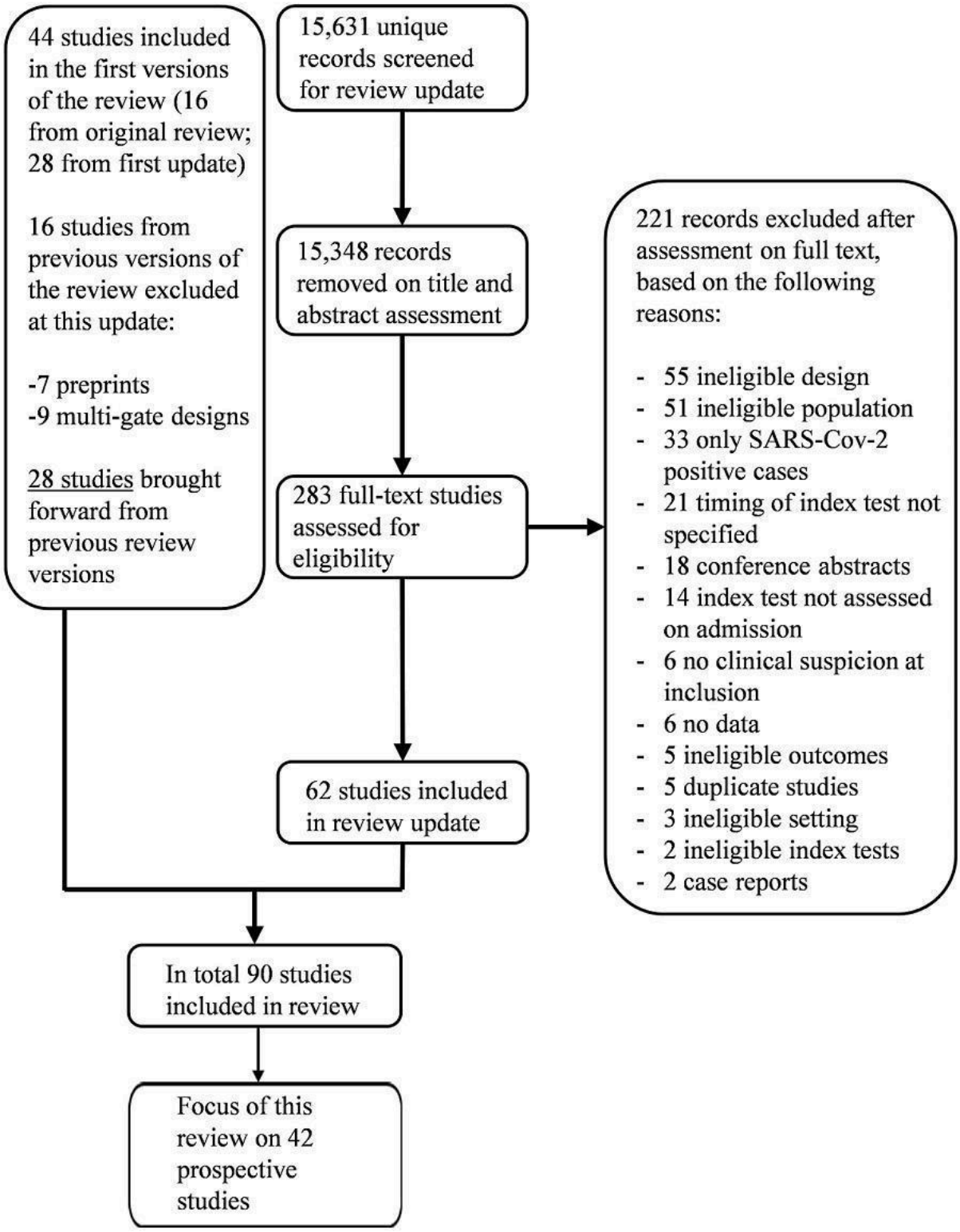
As we will explain in the discussion, this review will no longer be updated in its current form. Resources allowing, we will consider updating this review when sufficient studies of high methodological quality become available examining the combination of signs and symptoms with other, easy-to-obtain information such as demographics, point-of-care test results, prior exposure to an infected person, and recent case detection rate. Another important outcome would be to investigate whether tests exist that identify people requiring respiratory support (SARS or ARDS) or intensive care.

RESULTS

Results of the search

The first selection resulted in 23,683 potentially eligible articles. This included the 658 articles that we screened in our initial review and 7394 we screened in the first review update. After screening 15,631 articles on title and abstract for this update, we excluded 15,348 articles, leaving 283 full-text articles to be assessed. We included 90 studies in this version of the review, 28 of which were included in the previous reviews. We excluded 16 studies from the previous review versions from this review because they were either preprints of which no published version was available at the time of our final search (n = 7), or because they were case-control studies (multi-gate designs, n = 9); see Characteristics of excluded studies. The reasons for excluding 221 articles are listed in the flow chart (Figure 1; Moher 2009); reasons for excluding a selected number of studies (n = 143) that Cochrane readers might reasonably expect to find are also listed in Characteristics of excluded studies.

Figure 1. PRISMA flowchart



The participants in Zimmerman 2020 and Rutten 2020a were a subset of those included in Chung 2021 and Rutten 2020b, respectively. We included all four studies in this review, but we used only the more complete data from Chung 2021 and Rutten 2020b.

We determined the most appropriate data set in consultation with both study authors.

A summary of the main study characteristics of the prospective studies can be found in Table 2.

Methodological quality of included studies

The results of the quality assessment for all 90 included studies are summarised in Figure 2 and Figure 3. Of the 90 single-gate studies included in this review, 42 studies collected their data prospectively. Only one of the 48 retrospective studies applied a nested case-control design (Tordjman 2020).

Figure 2. Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies

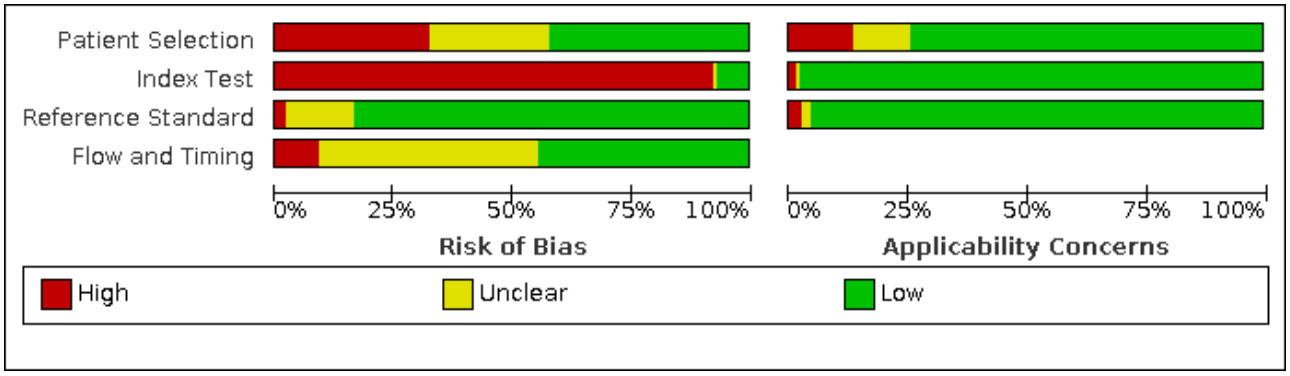


Figure 3. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study

Figure 3. (Continued)

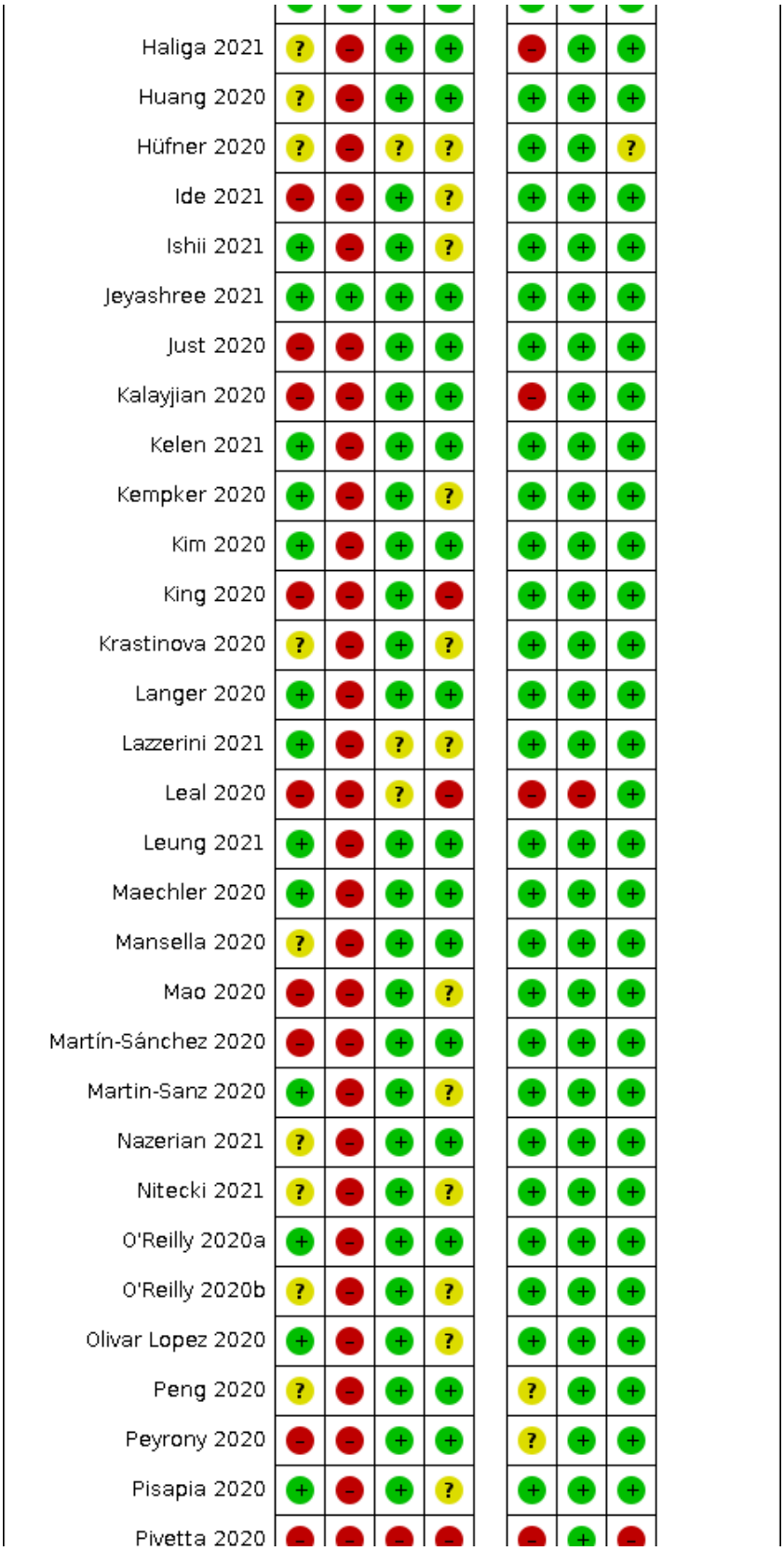


Figure 3. (Continued)

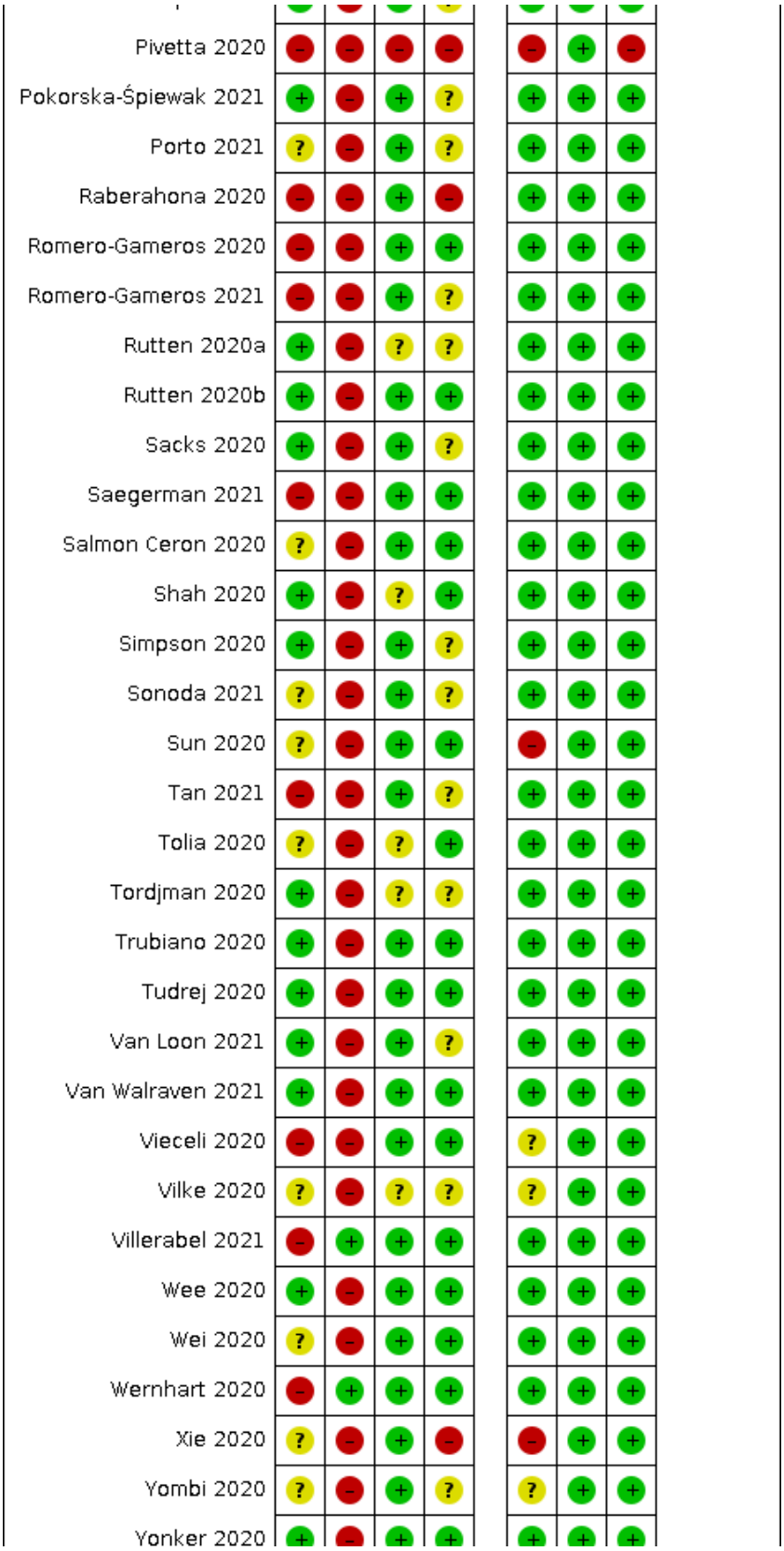
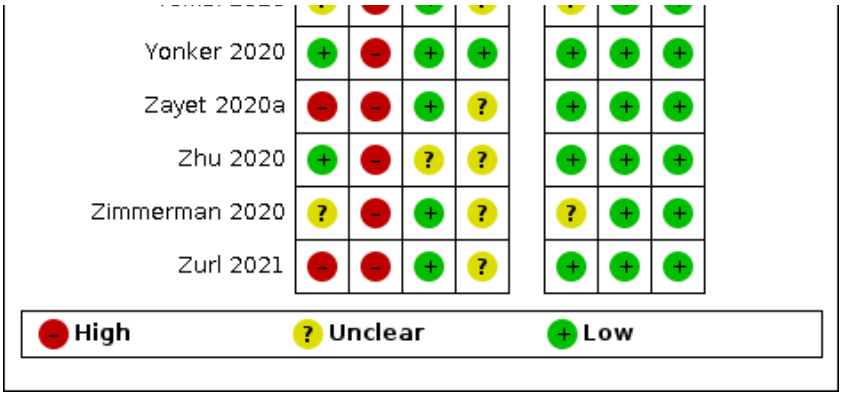


Figure 3. (Continued)



In the next section, we discuss the quality assessment of the 42 prospective studies only (Alizadehsani 2021; Bhattacharya 2021; Bouzid 2020; Brendish 2020; Buonafine 2020; Clemency 2020; Drager 2020; Fink 2021; Gilbert 2020; Haehner 2020; Ishii 2021; Jeyashree 2021; Just 2020; Kalayjian 2020; Kempker 2020; Krastinova 2020; Leal 2020; Maechler 2020; Mansella 2020; Martin-Sanz 2020; Nazerian 2021; O'Reilly 2020a; O'Reilly 2020b; Olivar Lopez 2020; Peyrony 2020; Pivetta 2020; Pokorska-Śpiewak 2021; Porto 2021; Romero-Gameros 2020; Romero-Gameros 2021; Rutten 2020a; Rutten 2020b; Saegerman 2021; Salmon Ceron 2020; Trubiano 2020; Tudrej 2020; Van Loon 2021; Van Walraven 2021; Villerabel 2021; Wee 2020; Wernhart 2020; Yonker 2020).

Participant selection

Participant selection was at high risk of bias in 12 out of 42 prospective studies. In seven studies (Alizadehsani 2021; Bhattacharya 2021; Brendish 2020; Buonafine 2020; Kalayjian 2020; Peyrony 2020; Romero-Gameros 2021), this was because a high level of preselection was used to decide whether RT-PCR testing was needed. For example, in Alizadehsani 2021, only patients with flu-like symptoms who were referred to the imaging department were included, leading to a preselection of individuals who are more likely to be infected with the SARS-CoV-2 virus and thus to a higher disease prevalence (38.5% in this example). Three studies (Bhattacharya 2021; Gilbert 2020; Just 2020), did not select a consecutive or random sample. Six studies (Leal 2020; Pivetta 2020; Romero-Gameros 2020; Saegerman 2021; Villerabel 2021; Wernhart 2020), excluded individuals while they were part of the study base.

For most studies, testing was dependent on the local case definition and testing criteria that was in effect at the time of the study, meaning all patients who were included in studies had already gone through a referral or selection filter.

Index tests

We rated all studies except seven (Bhattacharya 2021; Drager 2020; Fink 2021; Haehner 2020; Jeyashree 2021; Villerabel 2021; Wernhart 2020), as high risk of bias for the index tests because there was little to no detail on how, and by whom and when, the signs and symptoms were measured. However, concerns that the index tests, their performance or interpretation deviated from the research question were rated as low in all but one study (Leal 2020), where symptoms were ascertained via telephone assessment by a medical student. Olfactory symptoms were collected in different ways: interviews by telephone or in person using standardised questionnaires, online surveys, self-reporting at presentation, or systematic assessment by staff at enrolment without standardisation. The standardised questionnaires themselves are rarely reported, and are often newly developed by each research team.

Reference standard

We rated one study (Pivetta 2020), high risk of bias concerning the reference standard. They used either an RT-PCR or other information including clinical, lab data or imaging. All other studies used RT-PCR or CT scans, depending on the target condition, and we rated them low risk of bias, although some studies provided little detail on blinding. This lack of reporting of blinding of the reference standard did not result in a high risk of bias rating in studies with SARS-CoV-2 infection as the target condition, as we assumed that a lab-based RT-PCR result is not influenced by the index test results. Only one study (Alizadehsani 2021), was at unclear risk of bias because it was unclear whether the radiologist interpreting the CT scans was blinded to the index test results.

Flow and timing

Patient flow was unclear in 17 studies (Alizadehsani 2021; Bhattacharya 2021; Bouzid 2020; Brendish 2020; Buonafine 2020; Drager 2020; Ishii 2021; Kempker 2020; Krastinova 2020; Martin-Sanz 2020; O'Reilly 2020b; Olivar Lopez 2020; Pokorska-Śpiewak 2021; Porto 2021; Romero-Gameros 2021; Rutten 2020a; Van Loon 2021), either because the timing of recording signs and symptoms and conduct of the reference standard was unclear, or because some patients received a second or third reference standard at unclear time points during hospital admission, or because participant records were deleted when containing missing data. We rated two studies (Leal 2020; Pivetta 2020), high risk of bias concerning patient flow as not all participants received the same reference standard.

Overall ratings

In summary, we rated 36 of the 42 studies as high risk of bias for the index tests because there was little or no detail on how, by whom and when, the signs and symptoms were measured. Participant selection had a high risk of bias in 12 of the 42 studies. Risk of bias was most often rated low with regard to the implementation of the reference standard, and unclear with regard to flow and

timing. However, the applicability of the study findings to our review question did not often give rise to substantial concerns.

Findings

Findings: prospective studies

The main characteristics of all 42 prospective included studies are listed in Table 2.

Setting

Thirty-five studies were set in emergency departments or outpatient test centres (Alizadehsani 2021; Bhattacharya 2021; Bouzid 2020; Brendish 2020; Buonafine 2020; Clemency 2020; Drager 2020; Fink 2021; Gilbert 2020; Haehner 2020; Ishii 2021; Jeyashree 2021; Kalayjian 2020; Kempker 2020; Krastinova 2020; Leal 2020; Maechler 2020; Mansella 2020; Martin-Sanz 2020; Nazerian 2021; O'Reilly 2020a; O'Reilly 2020b; Olivar Lopez 2020; Peyrony 2020; Pivetta 2020; Porto 2021; Romero-Gameros 2020; Romero-Gameros 2021; Saegerman 2021; Salmon Ceron 2020; Trubiano 2020; Van Loon 2021; Van Walraven 2021; Villerabel 2021; Wee 2020), three studies in primary care settings (Just 2020; Tudrej 2020; Wernhart 2020), two studies in a mixed population of in- and outpatients in a hospital setting (Pokorska-Śpiewak 2021; Yonker 2020), and two overlapping studies in nursing homes (Rutten 2020a; Rutten 2020b).

Target conditions

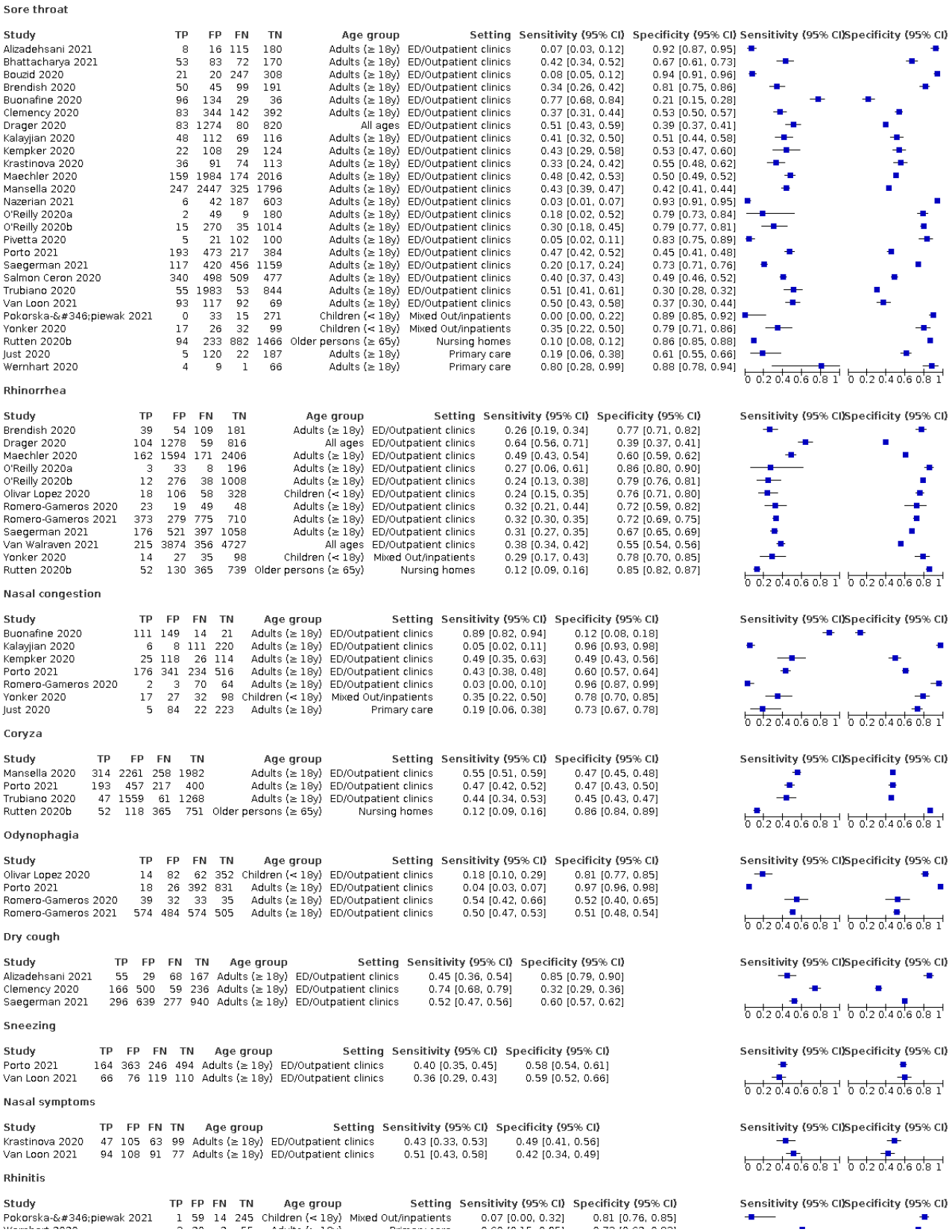
Only one study assessed accuracy of signs and symptoms for the diagnosis of COVID-19 pneumonia (Alizadehsani 2021), the remaining studies had SARS-CoV-2 infection as the target condition. The distinction between these two target conditions was not always very clear though, and a degree of overlap is to be assumed and we therefore present the results for both conditions together. All but two studies (Alizadehsani 2021; Drager 2020) used RT-PCR testing as reference standard, with some variation in the samples that were used. Alizadehsani 2021 used CT scanning for the diagnosis of COVID-19 pneumonia. Drager 2020 did not specify the reference standard.

General results

There were 52,608 participants in all 42 prospective studies, the median number of participants was 553. Prevalence varied from 3.7% to 60.6% with a median of 27.4%.

We found data on 96 symptoms, which fall into seven different categories,that is, systemic signs and symptoms, upper respiratory, lower respiratory, olfactory, gastro-intestinal, cardiovascular and multivariable combinations of signs or symptoms. Evidence on individual signs as diagnostic tests was rarely reported, so this review reports mainly on the diagnostic value of symptoms. Results for the prospective cross-sectional studies are presented in forest plots (Figure 4; Figure 5; Figure 6; Figure 7; Figure 8; Figure 9; Figure 10), and are plotted in ROC (receiver operating characteristic) space (Figure 11; Figure 12; Figure 13; Figure 14; Figure 15; Figure 16; Figure 17; Figure 18; Figure 19).

Figure 4. Forest plot of upper respiratory tract symptoms



Sore throat

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	8	16	115	180	Adults (≥ 18y)	ED/Outpatient clinics	0.07 [0.03, 0.12]	0.92 [0.87, 0.95]
Bhattacharya 2021	53	83	72	170	Adults (≥ 18y)	ED/Outpatient clinics	0.42 [0.34, 0.52]	0.67 [0.61, 0.73]
Bouzid 2020	21	20	247	308	Adults (≥ 18y)	ED/Outpatient clinics	0.08 [0.05, 0.12]	0.94 [0.91, 0.96]
Brendish 2020	50	45	99	191	Adults (≥ 18y)	ED/Outpatient clinics	0.34 [0.26, 0.42]	0.81 [0.75, 0.86]
Buonafine 2020	96	134	29	36	Adults (≥ 18y)	ED/Outpatient clinics	0.77 [0.68, 0.84]	0.21 [0.15, 0.28]
Clemency 2020	83	344	142	392	Adults (≥ 18y)	ED/Outpatient clinics	0.37 [0.31, 0.44]	0.53 [0.50, 0.57]
Drager 2020	83	1274	80	820	All ages	ED/Outpatient clinics	0.51 [0.43, 0.59]	0.39 [0.37, 0.41]
Kalayjian 2020	48	112	69	116	Adults (≥ 18y)	ED/Outpatient clinics	0.41 [0.32, 0.50]	0.51 [0.44, 0.58]
Kempker 2020	22	108	29	124	Adults (≥ 18y)	ED/Outpatient clinics	0.43 [0.29, 0.58]	0.53 [0.47, 0.60]
Krastinova 2020	36	91	74	113	Adults (≥ 18y)	ED/Outpatient clinics	0.33 [0.24, 0.42]	0.55 [0.48, 0.62]
Maechler 2020	159	1984	174	2016	Adults (≥ 18y)	ED/Outpatient clinics	0.48 [0.42, 0.53]	0.50 [0.49, 0.52]
Mansella 2020	247	2447	325	1796	Adults (≥ 18y)	ED/Outpatient clinics	0.43 [0.39, 0.47]	0.42 [0.41, 0.44]
Nazerian 2021	6	42	187	603	Adults (≥ 18y)	ED/Outpatient clinics	0.03 [0.01, 0.07]	0.93 [0.91, 0.95]
O'Reilly 2020a	2	49	9	180	Adults (≥ 18y)	ED/Outpatient clinics	0.18 [0.02, 0.52]	0.79 [0.73, 0.84]
O'Reilly 2020b	15	270	35	1014	Adults (≥ 18y)	ED/Outpatient clinics	0.30 [0.18, 0.45]	0.79 [0.77, 0.81]
Pivetta 2020	5	21	102	100	Adults (≥ 18y)	ED/Outpatient clinics	0.05 [0.02, 0.11]	0.83 [0.75, 0.89]
Porto 2021	193	473	217	384	Adults (≥ 18y)	ED/Outpatient clinics	0.47 [0.42, 0.52]	0.45 [0.41, 0.48]
Saegerman 2021	117	420	456	1159	Adults (≥ 18y)	ED/Outpatient clinics	0.20 [0.17, 0.24]	0.73 [0.71, 0.76]
Salmon Ceron 2020	340	498	509	477	Adults (≥ 18y)	ED/Outpatient clinics	0.40 [0.37, 0.43]	0.49 [0.46, 0.52]
Trubiano 2020	55	1983	53	844	Adults (≥ 18y)	ED/Outpatient clinics	0.51 [0.41, 0.61]	0.30 [0.28, 0.32]
Van Loon 2021	93	117	92	69	Adults (≥ 18y)	ED/Outpatient clinics	0.50 [0.43, 0.58]	0.37 [0.30, 0.44]
Pokorska-Śpiewak 2021	0	33	15	271	Children (< 18y)	Mixed Out/inpatients	0.00 [0.00, 0.22]	0.89 [0.85, 0.92]
Yonker 2020	17	26	32	99	Children (< 18y)	Mixed Out/inpatients	0.35 [0.22, 0.50]	0.79 [0.71, 0.86]
Rutten 2020b	94	233	882	1466	Older persons (≥ 65y)	Nursing homes	0.10 [0.08, 0.12]	0.86 [0.85, 0.88]
Just 2020	5	120	22	187	Adults (≥ 18y)	Primary care	0.19 [0.06, 0.38]	0.61 [0.55, 0.66]
Wernhart 2020	4	9	1	66	Adults (≥ 18y)	Primary care	0.80 [0.28, 0.99]	0.88 [0.78, 0.94]

Rhinorrhea

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Brendish 2020	39	54	109	181	Adults (≥ 18y)	ED/Outpatient clinics	0.26 [0.19, 0.34]	0.77 [0.71, 0.82]
Drager 2020	104	1278	59	816	All ages	ED/Outpatient clinics	0.64 [0.56, 0.71]	0.39 [0.37, 0.41]
Maechler 2020	162	1594	171	2406	Adults (≥ 18y)	ED/Outpatient clinics	0.49 [0.43, 0.54]	0.60 [0.59, 0.62]
O'Reilly 2020a	3	33	8	196	Adults (≥ 18y)	ED/Outpatient clinics	0.27 [0.06, 0.61]	0.86 [0.80, 0.90]
O'Reilly 2020b	12	276	38	1008	Adults (≥ 18y)	ED/Outpatient clinics	0.24 [0.13, 0.38]	0.79 [0.76, 0.81]
Olivar Lopez 2020	18	106	58	328	Children (< 18y)	ED/Outpatient clinics	0.24 [0.15, 0.35]	0.76 [0.71, 0.80]
Romero-Gameros 2020	23	19	49	48	Adults (≥ 18y)	ED/Outpatient clinics	0.32 [0.21, 0.44]	0.72 [0.59, 0.82]
Romero-Gameros 2021	373	279	775	710	Adults (≥ 18y)	ED/Outpatient clinics	0.32 [0.30, 0.35]	0.72 [0.69, 0.75]
Saegerman 2021	176	521	397	1058	Adults (≥ 18y)	ED/Outpatient clinics	0.31 [0.27, 0.35]	0.67 [0.65, 0.69]
Van Walraven 2021	215	3874	356	4727	All ages	ED/Outpatient clinics	0.38 [0.34, 0.42]	0.55 [0.54, 0.56]
Yonker 2020	14	27	35	98	Children (< 18y)	Mixed Out/inpatients	0.29 [0.17, 0.43]	0.78 [0.70, 0.85]
Rutten 2020b	52	130	365	739	Older persons (≥ 65y)	Nursing homes	0.12 [0.09, 0.16]	0.85 [0.82, 0.87]

Nasal congestion

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Buonafine 2020	111	149	14	21	Adults (≥ 18y)	ED/Outpatient clinics	0.89 [0.82, 0.94]	0.12 [0.08, 0.18]
Kalayjian 2020	6	8	111	220	Adults (≥ 18y)	ED/Outpatient clinics	0.05 [0.02, 0.11]	0.96 [0.93, 0.98]
Kempker 2020	25	118	26	114	Adults (≥ 18y)	ED/Outpatient clinics	0.49 [0.35, 0.63]	0.49 [0.43, 0.56]
Porto 2021	176	341	234	516	Adults (≥ 18y)	ED/Outpatient clinics	0.43 [0.38, 0.48]	0.60 [0.57, 0.64]
Romero-Gameros 2020	2	3	70	64	Adults (≥ 18y)	ED/Outpatient clinics	0.03 [0.00, 0.10]	0.96 [0.87, 0.99]
Yonker 2020	17	27	32	98	Children (< 18y)	Mixed Out/inpatients	0.35 [0.22, 0.50]	0.78 [0.70, 0.85]
Just 2020	5	84	22	223	Adults (≥ 18y)	Primary care	0.19 [0.06, 0.38]	0.73 [0.67, 0.78]

Coryza

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	314	2261	258	1982	Adults (≥ 18y)	ED/Outpatient clinics	0.55 [0.51, 0.59]	0.47 [0.45, 0.48]
Porto 2021	193	457	217	400	Adults (≥ 18y)	ED/Outpatient clinics	0.47 [0.42, 0.52]	0.47 [0.43, 0.50]
Trubiano 2020	47	1559	61	1268	Adults (≥ 18y)	ED/Outpatient clinics	0.44 [0.34, 0.53]	0.45 [0.43, 0.47]
Rutten 2020b	52	118	365	751	Older persons (≥ 65y)	Nursing homes	0.12 [0.09, 0.16]	0.86 [0.84, 0.89]

Odynophagia

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Olivar Lopez 2020	14	82	62	352	Children (< 18y)	ED/Outpatient clinics	0.18 [0.10, 0.29]	0.81 [0.77, 0.85]
Porto 2021	18	26	392	831	Adults (≥ 18y)	ED/Outpatient clinics	0.04 [0.03, 0.07]	0.97 [0.96, 0.98]
Romero-Gameros 2020	39	32	33	35	Adults (≥ 18y)	ED/Outpatient clinics	0.54 [0.42, 0.66]	0.52 [0.40, 0.65]
Romero-Gameros 2021	574	484	574	505	Adults (≥ 18y)	ED/Outpatient clinics	0.50 [0.47, 0.53]	0.51 [0.48, 0.54]

Dry cough

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	55	29	68	167	Adults (≥ 18y)	ED/Outpatient clinics	0.45 [0.36, 0.54]	0.85 [0.79, 0.90]
Clemency 2020	166	500	59	236	Adults (≥ 18y)	ED/Outpatient clinics	0.74 [0.68, 0.79]	0.32 [0.29, 0.36]
Saegerman 2021	296	639	277	940	Adults (≥ 18y)	ED/Outpatient clinics	0.52 [0.47, 0.56]	0.60 [0.57, 0.62]

Sneezing

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	164	363	246	494	Adults (≥ 18y)	ED/Outpatient clinics	0.40 [0.35, 0.45]	0.58 [0.54, 0.61]
Van Loon 2021	66	76	119	110	Adults (≥ 18y)	ED/Outpatient clinics	0.36 [0.29, 0.43]	0.59 [0.52, 0.66]

Nasal symptoms

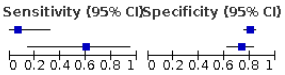
Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Krastinova 2020	47	105	63	99	Adults (≥ 18y)	ED/Outpatient clinics	0.43 [0.33, 0.53]	0.49 [0.41, 0.56]
Van Loon 2021	94	108	91	77	Adults (≥ 18y)	ED/Outpatient clinics	0.51 [0.43, 0.58]	0.42 [0.34, 0.49]

Rhinitis

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Pokorska-Śpiewak 2021	1	59	14	245	Children (< 18y)	Mixed Out/inpatients	0.07 [0.00, 0.32]	0.81 [0.76, 0.85]

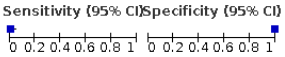
Figure 4. (Continued)

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Pokorska-Śpiewak 2021	1	59	14	245	Children (< 18y)	Mixed Out/inpatients	0.07 [0.00, 0.32]	0.81 [0.76, 0.85]
Wernhart 2020	3	20	2	55	Adults (≥ 18y)	Primary care	0.60 [0.15, 0.95]	0.73 [0.62, 0.83]



Sinusitis

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	1	13	107	2814	Adults (≥ 18y)	ED/Outpatient clinics	0.01 [0.00, 0.05]	1.00 [0.99, 1.00]



Expectoration

Study	TP	FP	FN	TN	Age group	Setting	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	12	27	256	301	Adults (≥ 18y)	ED/Outpatient clinics	0.04 [0.02, 0.08]	0.92 [0.88, 0.95]

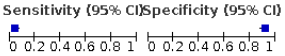
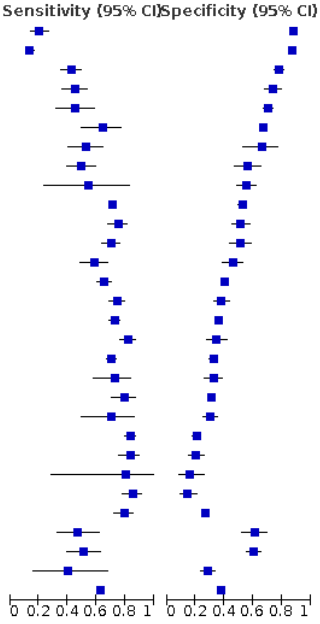


Figure 5. Forest plot of lower respiratory tract symptoms

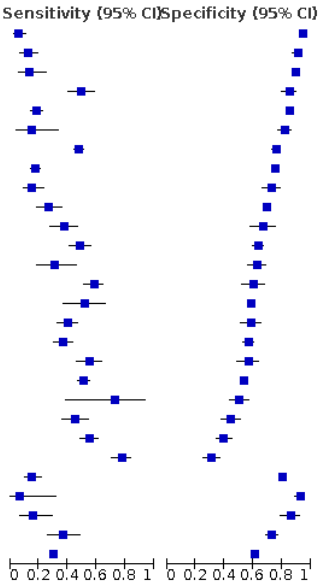
Cough

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Ishii 2021	33	416	131	2960	Adults (≥ 18y)	0.20 [0.14, 0.27]	0.88 [0.87, 0.89]
Saegerman 2021	78	210	495	1369	Adults (≥ 18y)	0.14 [0.11, 0.17]	0.87 [0.85, 0.88]
Nazerian 2021	82	142	111	503	Adults (≥ 18y)	0.42 [0.35, 0.50]	0.78 [0.75, 0.81]
Bhattacharya 2021	56	66	69	187	Adults (≥ 18y)	0.45 [0.36, 0.54]	0.74 [0.68, 0.79]
Villerabel 2021	26	223	32	528	Adults (≥ 18y)	0.45 [0.32, 0.58]	0.70 [0.67, 0.74]
O'Reilly 2020b	32	421	18	863	Adults (≥ 18y)	0.64 [0.49, 0.77]	0.67 [0.65, 0.70]
Romero-Gameros 2020	38	23	34	44	Adults (≥ 18y)	0.53 [0.41, 0.65]	0.66 [0.53, 0.77]
Pivetta 2020	53	53	54	68	Adults (≥ 18y)	0.50 [0.40, 0.59]	0.56 [0.47, 0.65]
O'Reilly 2020a	6	102	5	127	Adults (≥ 18y)	0.55 [0.23, 0.83]	0.55 [0.49, 0.62]
Romero-Gameros 2021	816	468	332	521	Adults (≥ 18y)	0.71 [0.68, 0.74]	0.53 [0.50, 0.56]
Brendish 2020	128	124	42	131	Adults (≥ 18y)	0.75 [0.68, 0.82]	0.51 [0.45, 0.58]
Peyrony 2020	158	81	67	85	Adults (≥ 18y)	0.70 [0.64, 0.76]	0.51 [0.43, 0.59]
Krastinova 2020	64	110	46	94	Adults (≥ 18y)	0.58 [0.48, 0.68]	0.46 [0.39, 0.53]
Maechler 2020	218	2405	115	1595	Adults (≥ 18y)	0.65 [0.60, 0.71]	0.40 [0.38, 0.41]
Bouzid 2020	199	203	69	125	Adults (≥ 18y)	0.74 [0.69, 0.79]	0.38 [0.33, 0.44]
Mansella 2020	415	2717	157	1526	Adults (≥ 18y)	0.73 [0.69, 0.76]	0.36 [0.35, 0.37]
Van Loon 2021	152	122	33	64	Adults (≥ 18y)	0.82 [0.76, 0.87]	0.34 [0.28, 0.42]
Salmon Ceron 2020	598	659	251	316	Adults (≥ 18y)	0.70 [0.67, 0.73]	0.32 [0.29, 0.35]
Kempker 2020	37	157	14	75	Adults (≥ 18y)	0.73 [0.58, 0.84]	0.32 [0.26, 0.39]
Trubiano 2020	86	1956	22	871	Adults (≥ 18y)	0.80 [0.71, 0.87]	0.31 [0.29, 0.33]
Just 2020	19	214	8	93	Adults (≥ 18y)	0.70 [0.50, 0.86]	0.30 [0.25, 0.36]
Porto 2021	343	678	67	179	Adults (≥ 18y)	0.84 [0.80, 0.87]	0.21 [0.18, 0.24]
Kalayjian 2020	98	181	19	47	Adults (≥ 18y)	0.84 [0.76, 0.90]	0.21 [0.16, 0.26]
Wernhart 2020	4	63	1	12	Adults (≥ 18y)	0.80 [0.28, 0.99]	0.16 [0.09, 0.26]
Buonafine 2020	107	145	18	25	Adults (≥ 18y)	0.86 [0.78, 0.91]	0.15 [0.10, 0.21]
Drager 2020	129	1527	34	567	All ages	0.79 [0.72, 0.85]	0.27 [0.25, 0.29]
Yonker 2020	23	49	26	76	Children (< 18y)	0.47 [0.33, 0.62]	0.61 [0.52, 0.69]
Olivar Lopez 2020	39	171	37	263	Children (< 18y)	0.51 [0.40, 0.63]	0.61 [0.56, 0.65]
Pokorska-Śpiewak 2021	6	217	9	87	Children (< 18y)	0.40 [0.16, 0.68]	0.29 [0.24, 0.34]
Rutten 2020b	917	1440	538	869	Older persons (≥ 65y)	0.63 [0.60, 0.66]	0.38 [0.36, 0.40]



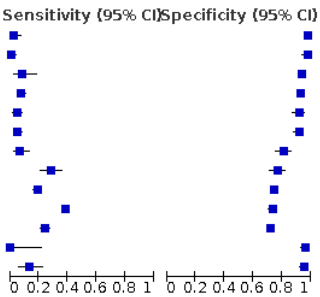
Dyspnoea

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Ishii 2021	10	176	154	3200	Adults (≥ 18y)	0.06 [0.03, 0.11]	0.95 [0.94, 0.96]
Bhattacharya 2021	16	23	109	230	Adults (≥ 18y)	0.13 [0.07, 0.20]	0.91 [0.87, 0.94]
Villerabel 2021	8	80	50	671	Adults (≥ 18y)	0.14 [0.06, 0.25]	0.89 [0.87, 0.91]
Alizadehsani 2021	61	29	62	167	Adults (≥ 18y)	0.50 [0.40, 0.59]	0.85 [0.79, 0.90]
Maechler 2020	61	597	272	3403	Adults (≥ 18y)	0.18 [0.14, 0.23]	0.85 [0.84, 0.86]
Just 2020	4	56	23	251	Adults (≥ 18y)	0.15 [0.04, 0.34]	0.82 [0.77, 0.86]
Romero-Gameros 2021	550	238	598	751	Adults (≥ 18y)	0.48 [0.45, 0.51]	0.76 [0.73, 0.79]
Mansella 2020	101	1057	471	3186	Adults (≥ 18y)	0.18 [0.15, 0.21]	0.75 [0.74, 0.76]
Krastinova 2020	17	55	93	149	Adults (≥ 18y)	0.15 [0.09, 0.24]	0.73 [0.66, 0.79]
Trubiano 2020	29	868	79	1959	Adults (≥ 18y)	0.27 [0.19, 0.36]	0.69 [0.68, 0.71]
Pivetta 2020	40	40	67	81	Adults (≥ 18y)	0.37 [0.28, 0.47]	0.67 [0.58, 0.75]
Nazerian 2021	94	237	99	408	Adults (≥ 18y)	0.49 [0.41, 0.56]	0.63 [0.59, 0.67]
Kempker 2020	16	86	35	146	Adults (≥ 18y)	0.31 [0.19, 0.46]	0.63 [0.56, 0.69]
Peyrony 2020	131	66	94	100	Adults (≥ 18y)	0.58 [0.51, 0.65]	0.60 [0.52, 0.68]
O'Reilly 2020b	26	529	24	755	Adults (≥ 18y)	0.52 [0.37, 0.66]	0.59 [0.56, 0.62]
Van Loon 2021	74	77	111	109	Adults (≥ 18y)	0.40 [0.33, 0.47]	0.59 [0.51, 0.66]
Clemency 2020	83	318	142	418	Adults (≥ 18y)	0.37 [0.31, 0.44]	0.57 [0.53, 0.60]
Buonafine 2020	69	74	56	96	Adults (≥ 18y)	0.55 [0.46, 0.64]	0.56 [0.49, 0.64]
Saegerman 2021	293	729	280	850	Adults (≥ 18y)	0.51 [0.47, 0.55]	0.54 [0.51, 0.56]
O'Reilly 2020a	8	114	3	115	Adults (≥ 18y)	0.73 [0.39, 0.94]	0.50 [0.44, 0.57]
Kalayjian 2020	53	126	64	102	Adults (≥ 18y)	0.45 [0.36, 0.55]	0.45 [0.38, 0.51]
Bouzid 2020	147	198	121	130	Adults (≥ 18y)	0.55 [0.49, 0.61]	0.40 [0.34, 0.45]
Brendish 2020	130	179	38	81	Adults (≥ 18y)	0.77 [0.70, 0.83]	0.31 [0.26, 0.37]
Drager 2020	25	411	138	1683	All ages	0.15 [0.10, 0.22]	0.80 [0.79, 0.82]
Pokorska-Śpiewak 2021	1	23	14	281	Children (< 18y)	0.07 [0.00, 0.32]	0.92 [0.89, 0.95]
Yonker 2020	8	17	41	108	Children (< 18y)	0.16 [0.07, 0.30]	0.86 [0.79, 0.92]
Olivar Lopez 2020	28	117	48	317	Children (< 18y)	0.37 [0.26, 0.49]	0.73 [0.69, 0.77]
Rutten 2020b	417	882	956	1367	Older persons (≥ 65y)	0.30 [0.28, 0.33]	0.61 [0.59, 0.63]



Chest tightness/pain

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	3	68	105	2759	Adults (≥ 18y)	0.03 [0.01, 0.08]	0.98 [0.97, 0.98]
Alizadehsani 2021	1	5	122	191	Adults (≥ 18y)	0.01 [0.00, 0.04]	0.97 [0.94, 0.99]
Villerabel 2021	5	47	53	704	Adults (≥ 18y)	0.09 [0.03, 0.19]	0.94 [0.92, 0.95]
Maechler 2020	26	308	307	3692	Adults (≥ 18y)	0.08 [0.05, 0.11]	0.92 [0.91, 0.93]
Peyrony 2020	11	13	214	153	Adults (≥ 18y)	0.05 [0.02, 0.09]	0.92 [0.87, 0.96]
Bouzid 2020	15	28	253	300	Adults (≥ 18y)	0.06 [0.03, 0.09]	0.91 [0.88, 0.94]
Krastinova 2020	8	38	102	166	Adults (≥ 18y)	0.07 [0.03, 0.14]	0.81 [0.75, 0.86]
Brendish 2020	43	55	107	187	Adults (≥ 18y)	0.29 [0.22, 0.37]	0.77 [0.71, 0.82]
Saegerman 2021	109	401	464	1178	Adults (≥ 18y)	0.19 [0.16, 0.22]	0.75 [0.72, 0.77]
Romero-Gameros 2021	445	263	703	726	Adults (≥ 18y)	0.39 [0.36, 0.42]	0.73 [0.71, 0.76]
Mansella 2020	139	1196	433	3047	Adults (≥ 18y)	0.24 [0.21, 0.28]	0.72 [0.70, 0.73]
Pokorska-Śpiewak 2021	0	12	15	292	Children (< 18y)	0.00 [0.00, 0.22]	0.96 [0.93, 0.98]
Olivar Lopez 2020	10	22	66	412	Children (< 18y)	0.13 [0.06, 0.23]	0.95 [0.92, 0.97]

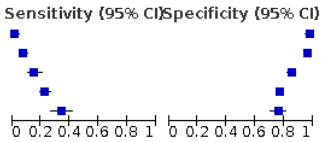


Sputum production/productive cough

Figure 5. (Continued)

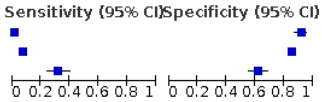
Sputum production/productive cough

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	2	4	121	192	Adults (≥ 18y)	0.02 [0.00, 0.06]	0.98 [0.95, 0.99]
Porto 2021	32	34	378	823	Adults (≥ 18y)	0.08 [0.05, 0.11]	0.96 [0.94, 0.97]
Clemency 2020	35	111	190	625	Adults (≥ 18y)	0.16 [0.11, 0.21]	0.85 [0.82, 0.87]
Mansella 2020	132	987	440	3256	Adults (≥ 18y)	0.23 [0.20, 0.27]	0.77 [0.75, 0.78]
Brendish 2020	53	56	101	181	Adults (≥ 18y)	0.34 [0.27, 0.42]	0.76 [0.70, 0.82]



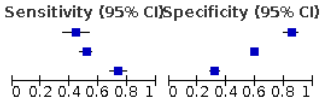
Wheeze

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	4	13	221	153	Adults (≥ 18y)	0.02 [0.00, 0.04]	0.92 [0.87, 0.96]
Mansella 2020	42	633	530	3610	Adults (≥ 18y)	0.07 [0.05, 0.10]	0.85 [0.84, 0.86]
Brendish 2020	48	91	102	150	Adults (≥ 18y)	0.32 [0.25, 0.40]	0.62 [0.56, 0.68]



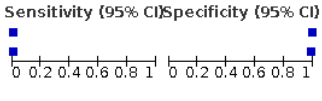
Dry cough

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	55	29	68	167	Adults (≥ 18y)	0.45 [0.36, 0.54]	0.85 [0.79, 0.90]
Saegerman 2021	296	639	277	940	Adults (≥ 18y)	0.52 [0.47, 0.56]	0.60 [0.57, 0.62]
Clemency 2020	166	500	59	236	Adults (≥ 18y)	0.74 [0.68, 0.79]	0.32 [0.29, 0.36]



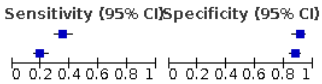
Haemoptysis

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	3	1	222	165	Adults (≥ 18y)	0.01 [0.00, 0.04]	0.99 [0.97, 1.00]
Mansella 2020	4	49	568	4194	Adults (≥ 18y)	0.01 [0.00, 0.02]	0.99 [0.98, 0.99]



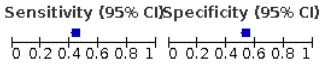
Pulmonary auscultation: crackling bilateral

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	80	15	145	151	Adults (≥ 18y)	0.36 [0.29, 0.42]	0.91 [0.86, 0.95]
Bouzid 2020	53	39	215	289	Adults (≥ 18y)	0.20 [0.15, 0.25]	0.88 [0.84, 0.91]



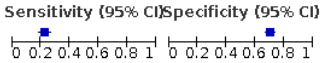
Hypoxia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Rutten 2020b	453	820	570	931	Older persons (≥ 65y)	0.44 [0.41, 0.47]	0.53 [0.51, 0.56]



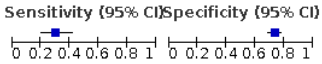
Respiratory distress

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	94	252	316	605	Adults (≥ 18y)	0.23 [0.19, 0.27]	0.71 [0.67, 0.74]



Tachypnoea

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Olivar Lopez 2020	23	115	53	319	Children (< 18y)	0.30 [0.20, 0.42]	0.74 [0.69, 0.78]



Pulmonary auscultation: crackling unilateral

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	21	12	204	154	Adults (≥ 18y)	0.09 [0.06, 0.14]	0.93 [0.88, 0.96]

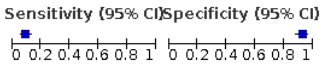
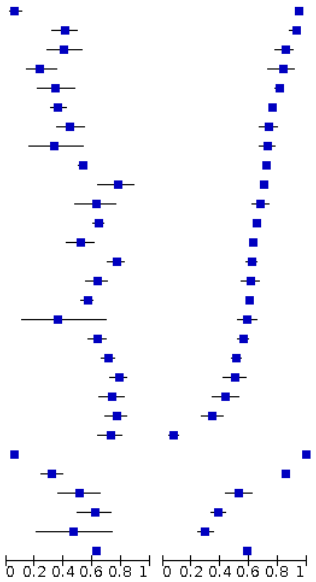


Figure 6. Forest plot of systemic signs and symptoms

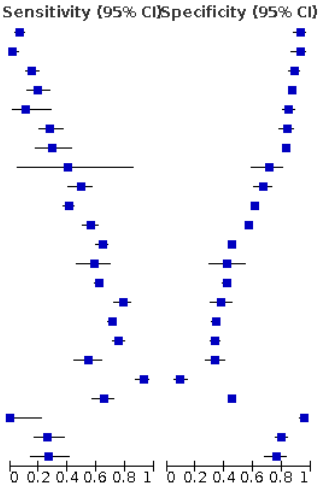
Fever

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Ishii 2021	10	184	154	3192	Adults (≥ 18y)	0.06 [0.03, 0.11]	0.95 [0.94, 0.95]
Alizadehsani 2021	50	15	73	181	Adults (≥ 18y)	0.41 [0.32, 0.50]	0.92 [0.88, 0.96]
Fink 2021	29	22	43	125	Adults (≥ 18y)	0.40 [0.29, 0.53]	0.85 [0.78, 0.90]
Romero-Gameros 2020	17	11	55	56	Adults (≥ 18y)	0.24 [0.14, 0.35]	0.84 [0.73, 0.92]
Villerabel 2021	20	142	38	609	Adults (≥ 18y)	0.34 [0.22, 0.48]	0.81 [0.78, 0.84]
Maechler 2020	121	968	212	3032	Adults (≥ 18y)	0.36 [0.31, 0.42]	0.76 [0.74, 0.77]
Krastinova 2020	49	54	61	150	Adults (≥ 18y)	0.45 [0.35, 0.54]	0.74 [0.67, 0.79]
Just 2020	9	84	18	223	Adults (≥ 18y)	0.33 [0.17, 0.54]	0.73 [0.67, 0.78]
Romero-Gameros 2021	615	276	533	713	Adults (≥ 18y)	0.54 [0.51, 0.56]	0.72 [0.69, 0.75]
O'Reilly 2020b	39	383	11	901	Adults (≥ 18y)	0.78 [0.64, 0.88]	0.70 [0.68, 0.73]
Kempker 2020	32	74	19	158	Adults (≥ 18y)	0.63 [0.48, 0.76]	0.68 [0.62, 0.74]
Saegerman 2021	368	550	205	1029	Adults (≥ 18y)	0.64 [0.60, 0.68]	0.65 [0.63, 0.68]
Trubiano 2020	56	1063	52	1764	Adults (≥ 18y)	0.52 [0.42, 0.62]	0.62 [0.61, 0.64]
Nazerian 2021	148	247	45	398	Adults (≥ 18y)	0.77 [0.70, 0.82]	0.62 [0.58, 0.65]
Brendish 2020	103	97	60	152	Adults (≥ 18y)	0.63 [0.55, 0.71]	0.61 [0.55, 0.67]
Mansella 2020	323	1689	249	2554	Adults (≥ 18y)	0.56 [0.52, 0.61]	0.60 [0.59, 0.62]
O'Reilly 2020a	4	94	7	135	Adults (≥ 18y)	0.36 [0.11, 0.69]	0.59 [0.52, 0.65]
Clemency 2020	143	323	82	413	Adults (≥ 18y)	0.64 [0.57, 0.70]	0.56 [0.52, 0.60]
Porto 2021	291	420	119	437	Adults (≥ 18y)	0.71 [0.66, 0.75]	0.51 [0.48, 0.54]
Peyrony 2020	176	83	49	83	Adults (≥ 18y)	0.78 [0.72, 0.83]	0.50 [0.42, 0.58]
Pivetta 2020	79	68	28	53	Adults (≥ 18y)	0.74 [0.64, 0.82]	0.44 [0.35, 0.53]
Buonafine 2020	96	112	29	58	Adults (≥ 18y)	0.77 [0.68, 0.84]	0.34 [0.27, 0.42]
Bhattacharya 2021	91	234	34	19	Adults (≥ 18y)	0.73 [0.64, 0.80]	0.08 [0.05, 0.11]
Van Walraven 2021	36	71	535	8530	All ages	0.06 [0.04, 0.09]	0.99 [0.99, 0.99]
Drager 2020	52	310	111	1784	All ages	0.32 [0.25, 0.40]	0.85 [0.84, 0.87]
Yonker 2020	25	59	24	66	Children (< 18y)	0.51 [0.36, 0.66]	0.53 [0.44, 0.62]
Olivar Lopez 2020	47	266	29	168	Children (< 18y)	0.62 [0.50, 0.73]	0.39 [0.34, 0.43]
Pokorska-Śpiewak 2021	7	214	8	90	Children (< 18y)	0.47 [0.21, 0.73]	0.30 [0.25, 0.35]
Rutten 2020b	917	969	538	1347	Older persons (≥ 65y)	0.63 [0.60, 0.66]	0.58 [0.56, 0.60]



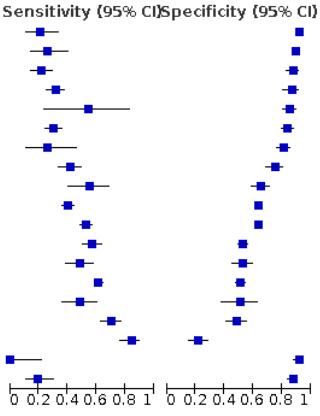
Headache

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	15	12	210	154	Adults (≥ 18y)	0.07 [0.04, 0.11]	0.93 [0.88, 0.96]
Pivetta 2020	2	9	105	112	Adults (≥ 18y)	0.02 [0.00, 0.07]	0.93 [0.86, 0.97]
Bouzid 2020	41	37	227	291	Adults (≥ 18y)	0.15 [0.11, 0.20]	0.89 [0.85, 0.92]
Trubiano 2020	21	381	87	2446	Adults (≥ 18y)	0.19 [0.12, 0.28]	0.87 [0.85, 0.88]
Just 2020	3	47	24	260	Adults (≥ 18y)	0.11 [0.02, 0.29]	0.85 [0.80, 0.89]
Bhattacharya 2021	35	42	90	211	Adults (≥ 18y)	0.28 [0.20, 0.37]	0.83 [0.78, 0.88]
Villerabel 2021	17	128	41	623	Adults (≥ 18y)	0.29 [0.18, 0.43]	0.83 [0.80, 0.86]
Wernhart 2020	2	22	3	53	Adults (≥ 18y)	0.40 [0.05, 0.85]	0.71 [0.59, 0.81]
Brendish 2020	73	78	76	157	Adults (≥ 18y)	0.49 [0.41, 0.57]	0.67 [0.60, 0.73]
Saegerman 2021	234	614	339	965	Adults (≥ 18y)	0.41 [0.37, 0.45]	0.61 [0.59, 0.64]
Maechler 2020	187	1713	146	2287	Adults (≥ 18y)	0.56 [0.51, 0.62]	0.57 [0.56, 0.59]
Mansella 2020	366	2327	206	1916	Adults (≥ 18y)	0.64 [0.60, 0.68]	0.45 [0.44, 0.47]
Romero-Gameros 2020	42	39	30	28	Adults (≥ 18y)	0.58 [0.46, 0.70]	0.42 [0.30, 0.54]
Romero-Gameros 2021	709	578	439	411	Adults (≥ 18y)	0.62 [0.59, 0.65]	0.42 [0.38, 0.45]
Van Loon 2021	145	116	40	70	Adults (≥ 18y)	0.78 [0.72, 0.84]	0.38 [0.31, 0.45]
Salmon Ceron 2020	603	640	246	335	Adults (≥ 18y)	0.71 [0.68, 0.74]	0.34 [0.31, 0.37]
Porto 2021	310	570	100	287	Adults (≥ 18y)	0.76 [0.71, 0.80]	0.33 [0.30, 0.37]
Krastinova 2020	60	136	50	68	Adults (≥ 18y)	0.55 [0.45, 0.64]	0.33 [0.27, 0.40]
Buonafine 2020	116	154	9	16	Adults (≥ 18y)	0.93 [0.87, 0.97]	0.09 [0.05, 0.15]
Drager 2020	106	1151	57	943	All ages	0.65 [0.57, 0.72]	0.45 [0.43, 0.47]
Pokorska-Śpiewak 2021	0	15	15	289	Children (< 18y)	0.00 [0.00, 0.22]	0.95 [0.92, 0.97]
Olivar Lopez 2020	20	88	56	346	Children (< 18y)	0.26 [0.17, 0.38]	0.80 [0.76, 0.83]
Yonker 2020	13	30	36	95	Children (< 18y)	0.27 [0.15, 0.41]	0.76 [0.68, 0.83]



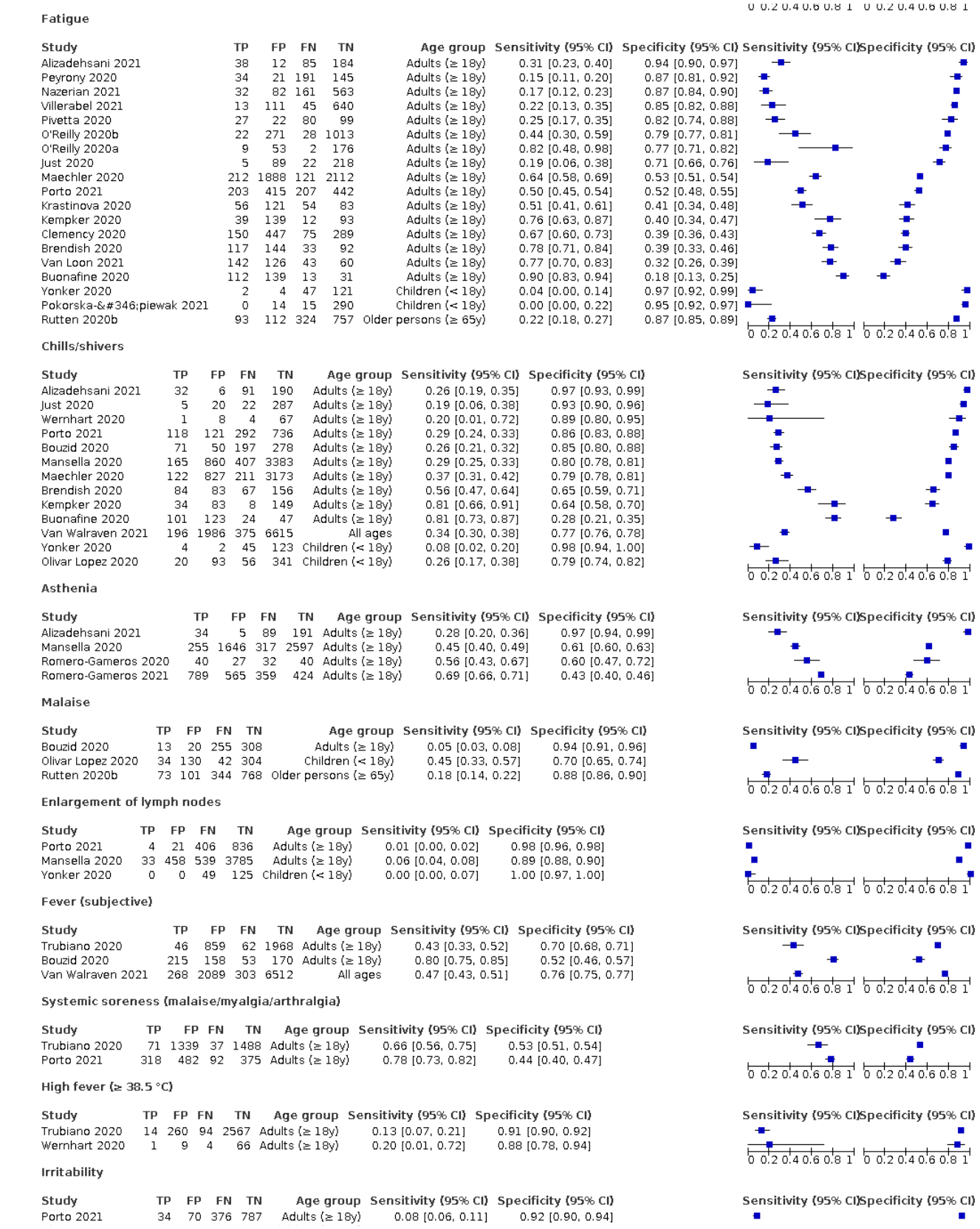
Myalgia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Villerabel 2021	12	58	46	693	Adults (≥ 18y)	0.21 [0.11, 0.33]	0.92 [0.90, 0.94]
O'Reilly 2020b	13	139	37	1145	Adults (≥ 18y)	0.26 [0.15, 0.40]	0.89 [0.87, 0.91]
Bhattacharya 2021	27	31	98	222	Adults (≥ 18y)	0.22 [0.15, 0.30]	0.88 [0.83, 0.92]
Peyrony 2020	71	22	154	144	Adults (≥ 18y)	0.32 [0.26, 0.38]	0.87 [0.81, 0.92]
O'Reilly 2020a	6	33	5	196	Adults (≥ 18y)	0.55 [0.23, 0.83]	0.86 [0.80, 0.90]
Bouzid 2020	81	53	187	275	Adults (≥ 18y)	0.30 [0.25, 0.36]	0.84 [0.79, 0.88]
Just 2020	7	59	20	248	Adults (≥ 18y)	0.26 [0.11, 0.46]	0.81 [0.76, 0.85]
Brendish 2020	62	58	87	174	Adults (≥ 18y)	0.42 [0.34, 0.50]	0.75 [0.69, 0.80]
Kempker 2020	28	80	23	152	Adults (≥ 18y)	0.55 [0.40, 0.69]	0.66 [0.59, 0.72]
Saegerman 2021	230	570	343	1009	Adults (≥ 18y)	0.40 [0.36, 0.44]	0.64 [0.61, 0.66]
Mansella 2020	301	1558	271	2685	Adults (≥ 18y)	0.53 [0.48, 0.57]	0.63 [0.62, 0.65]
Clemency 2020	128	347	97	389	Adults (≥ 18y)	0.57 [0.50, 0.63]	0.53 [0.49, 0.57]
Krastinova 2020	53	97	57	107	Adults (≥ 18y)	0.48 [0.39, 0.58]	0.52 [0.45, 0.59]
Romero-Gameros 2021	705	483	443	506	Adults (≥ 18y)	0.61 [0.59, 0.64]	0.51 [0.48, 0.54]
Romero-Gameros 2020	35	33	37	34	Adults (≥ 18y)	0.49 [0.37, 0.61]	0.51 [0.38, 0.63]
Van Loon 2021	130	96	55	90	Adults (≥ 18y)	0.70 [0.63, 0.77]	0.48 [0.41, 0.56]
Buonafine 2020	105	133	20	37	Adults (≥ 18y)	0.84 [0.76, 0.90]	0.22 [0.16, 0.29]
Pokorska-Śpiewak 2021	0	25	15	279	Children (< 18y)	0.00 [0.00, 0.22]	0.92 [0.88, 0.95]
Olivar Lopez 2020	15	54	61	380	Children (< 18y)	0.20 [0.11, 0.30]	0.88 [0.84, 0.91]



Fatigue

Figure 6. (Continued)



Fatigue

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	38	12	85	184	Adults (≥ 18y)	0.31 [0.23, 0.40]	0.94 [0.90, 0.97]
Peyrony 2020	34	21	191	145	Adults (≥ 18y)	0.15 [0.11, 0.20]	0.87 [0.81, 0.92]
Nazerian 2021	32	82	161	563	Adults (≥ 18y)	0.17 [0.12, 0.23]	0.87 [0.84, 0.90]
Villerabel 2021	13	111	45	640	Adults (≥ 18y)	0.22 [0.13, 0.35]	0.85 [0.82, 0.88]
Pivetta 2020	27	22	80	99	Adults (≥ 18y)	0.25 [0.17, 0.35]	0.82 [0.74, 0.88]
O'Reilly 2020b	22	271	28	1013	Adults (≥ 18y)	0.44 [0.30, 0.59]	0.79 [0.77, 0.81]
O'Reilly 2020a	9	53	2	176	Adults (≥ 18y)	0.82 [0.48, 0.98]	0.77 [0.71, 0.82]
Just 2020	5	89	22	218	Adults (≥ 18y)	0.19 [0.06, 0.38]	0.71 [0.66, 0.76]
Maechler 2020	212	1888	121	2112	Adults (≥ 18y)	0.64 [0.58, 0.69]	0.53 [0.51, 0.54]
Porto 2021	203	415	207	442	Adults (≥ 18y)	0.50 [0.45, 0.54]	0.52 [0.48, 0.55]
Krastinova 2020	56	121	54	83	Adults (≥ 18y)	0.51 [0.41, 0.61]	0.41 [0.34, 0.48]
Kempker 2020	39	139	12	93	Adults (≥ 18y)	0.76 [0.63, 0.87]	0.40 [0.34, 0.47]
Clemency 2020	150	447	75	289	Adults (≥ 18y)	0.67 [0.60, 0.73]	0.39 [0.36, 0.43]
Brendish 2020	117	144	33	92	Adults (≥ 18y)	0.78 [0.71, 0.84]	0.39 [0.33, 0.46]
Van Loon 2021	142	126	43	60	Adults (≥ 18y)	0.77 [0.70, 0.83]	0.32 [0.26, 0.39]
Buonafine 2020	112	139	13	31	Adults (≥ 18y)	0.90 [0.83, 0.94]	0.18 [0.13, 0.25]
Yonker 2020	2	4	47	121	Children (< 18y)	0.04 [0.00, 0.14]	0.97 [0.92, 0.99]
Pokorska-Śpiewak 2021	0	14	15	290	Children (< 18y)	0.00 [0.00, 0.22]	0.95 [0.92, 0.97]
Rutten 2020b	93	112	324	757	Older persons (≥ 65y)	0.22 [0.18, 0.27]	0.87 [0.85, 0.89]

Chills/shivers

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	32	6	91	190	Adults (≥ 18y)	0.26 [0.19, 0.35]	0.97 [0.93, 0.99]
Just 2020	5	20	22	287	Adults (≥ 18y)	0.19 [0.06, 0.38]	0.93 [0.90, 0.96]
Wernhart 2020	1	8	4	67	Adults (≥ 18y)	0.20 [0.01, 0.72]	0.89 [0.80, 0.95]
Porto 2021	118	121	292	736	Adults (≥ 18y)	0.29 [0.24, 0.33]	0.86 [0.83, 0.88]
Bouzid 2020	71	50	197	278	Adults (≥ 18y)	0.26 [0.21, 0.32]	0.85 [0.80, 0.88]
Mansella 2020	165	860	407	3383	Adults (≥ 18y)	0.29 [0.25, 0.33]	0.80 [0.78, 0.81]
Maechler 2020	122	827	211	3173	Adults (≥ 18y)	0.37 [0.31, 0.42]	0.79 [0.78, 0.81]
Brendish 2020	84	83	67	156	Adults (≥ 18y)	0.56 [0.47, 0.64]	0.65 [0.59, 0.71]
Kempker 2020	34	83	8	149	Adults (≥ 18y)	0.81 [0.66, 0.91]	0.64 [0.58, 0.70]
Buonafine 2020	101	123	24	47	Adults (≥ 18y)	0.81 [0.73, 0.87]	0.28 [0.21, 0.35]
Van Walraven 2021	196	1986	375	6615	All ages	0.34 [0.30, 0.38]	0.77 [0.76, 0.78]
Yonker 2020	4	2	45	123	Children (< 18y)	0.08 [0.02, 0.20]	0.98 [0.94, 1.00]
Olivar Lopez 2020	20	93	56	341	Children (< 18y)	0.26 [0.17, 0.38]	0.79 [0.74, 0.82]

Asthenia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	34	5	89	191	Adults (≥ 18y)	0.28 [0.20, 0.36]	0.97 [0.94, 0.99]
Mansella 2020	255	1646	317	2597	Adults (≥ 18y)	0.45 [0.40, 0.49]	0.61 [0.60, 0.63]
Romero-Gameros 2020	40	27	32	40	Adults (≥ 18y)	0.56 [0.43, 0.67]	0.60 [0.47, 0.72]
Romero-Gameros 2021	789	565	359	424	Adults (≥ 18y)	0.69 [0.66, 0.71]	0.43 [0.40, 0.46]

Malaise

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	13	20	255	308	Adults (≥ 18y)	0.05 [0.03, 0.08]	0.94 [0.91, 0.96]
Olivar Lopez 2020	34	130	42	304	Children (< 18y)	0.45 [0.33, 0.57]	0.70 [0.65, 0.74]
Rutten 2020b	73	101	344	768	Older persons (≥ 65y)	0.18 [0.14, 0.22]	0.88 [0.86, 0.90]

Enlargement of lymph nodes

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	4	21	406	836	Adults (≥ 18y)	0.01 [0.00, 0.02]	0.98 [0.96, 0.98]
Mansella 2020	33	458	539	3785	Adults (≥ 18y)	0.06 [0.04, 0.08]	0.89 [0.88, 0.90]
Yonker 2020	0	0	49	125	Children (< 18y)	0.00 [0.00, 0.07]	1.00 [0.97, 1.00]

Fever (subjective)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	46	859	62	1968	Adults (≥ 18y)	0.43 [0.33, 0.52]	0.70 [0.68, 0.71]
Bouzid 2020	215	158	53	170	Adults (≥ 18y)	0.80 [0.75, 0.85]	0.52 [0.46, 0.57]
Van Walraven 2021	268	2089	303	6512	All ages	0.47 [0.43, 0.51]	0.76 [0.75, 0.77]

Systemic soreness (malaise/myalgia/arthralgia)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	71	1339	37	1488	Adults (≥ 18y)	0.66 [0.56, 0.75]	0.53 [0.51, 0.54]
Porto 2021	318	482	92	375	Adults (≥ 18y)	0.78 [0.73, 0.82]	0.44 [0.40, 0.47]

High fever (≥ 38.5 °C)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	14	260	94	2567	Adults (≥ 18y)	0.13 [0.07, 0.21]	0.91 [0.90, 0.92]
Wernhart 2020	1	9	4	66	Adults (≥ 18y)	0.20 [0.01, 0.72]	0.88 [0.78, 0.94]

Irritability

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	34	70	376	787	Adults (≥ 18y)	0.08 [0.06, 0.11]	0.92 [0.90, 0.94]

Figure 6. (Continued)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	34	70	376	787	Adults (≥ 18y)	0.08 [0.06, 0.11]	0.92 [0.90, 0.94]
Olivar Lopez 2020	26	154	50	280	Children (< 18y)	0.34 [0.24, 0.46]	0.65 [0.60, 0.69]

Loss of appetite

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Clemency 2020	90	194	135	542	Adults (≥ 18y)	0.40 [0.34, 0.47]	0.74 [0.70, 0.77]
Brendish 2020	112	116	40	116	Adults (≥ 18y)	0.74 [0.66, 0.80]	0.50 [0.43, 0.57]

Sweating

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	15	2	108	194	Adults (≥ 18y)	0.12 [0.07, 0.19]	0.99 [0.96, 1.00]
Bouzid 2020	29	29	239	299	Adults (≥ 18y)	0.11 [0.07, 0.15]	0.91 [0.88, 0.94]

Rigors

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	76	546	495	8055	All ages	0.13 [0.11, 0.16]	0.94 [0.93, 0.94]

Exhaustion

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	271	1860	301	2383	Adults (≥ 18y)	0.47 [0.43, 0.52]	0.56 [0.55, 0.58]

Isolated fever

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	5	7	170	416	Adults (≥ 18y)	0.03 [0.01, 0.07]	0.98 [0.97, 0.99]

Isolated headache

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	0	3	175	420	Adults (≥ 18y)	0.00 [0.00, 0.02]	0.99 [0.98, 1.00]

Low body temperature

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	6	13	262	315	Adults (≥ 18y)	0.02 [0.01, 0.05]	0.96 [0.93, 0.98]

Dizziness

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	11	0	112	196	Adults (≥ 18y)	0.09 [0.05, 0.15]	1.00 [0.98, 1.00]

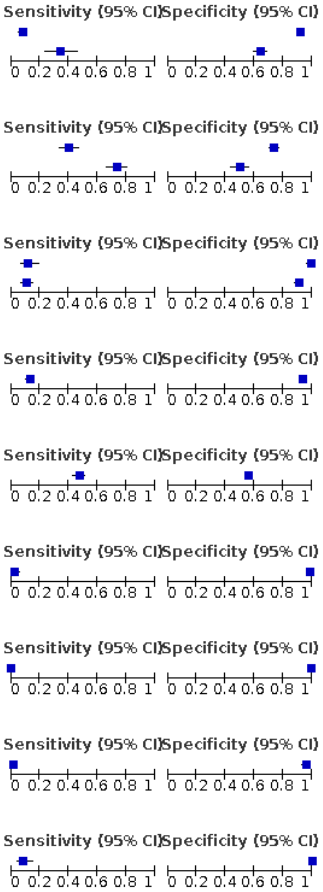


Figure 7. Forest plot of gastrointestinal symptoms

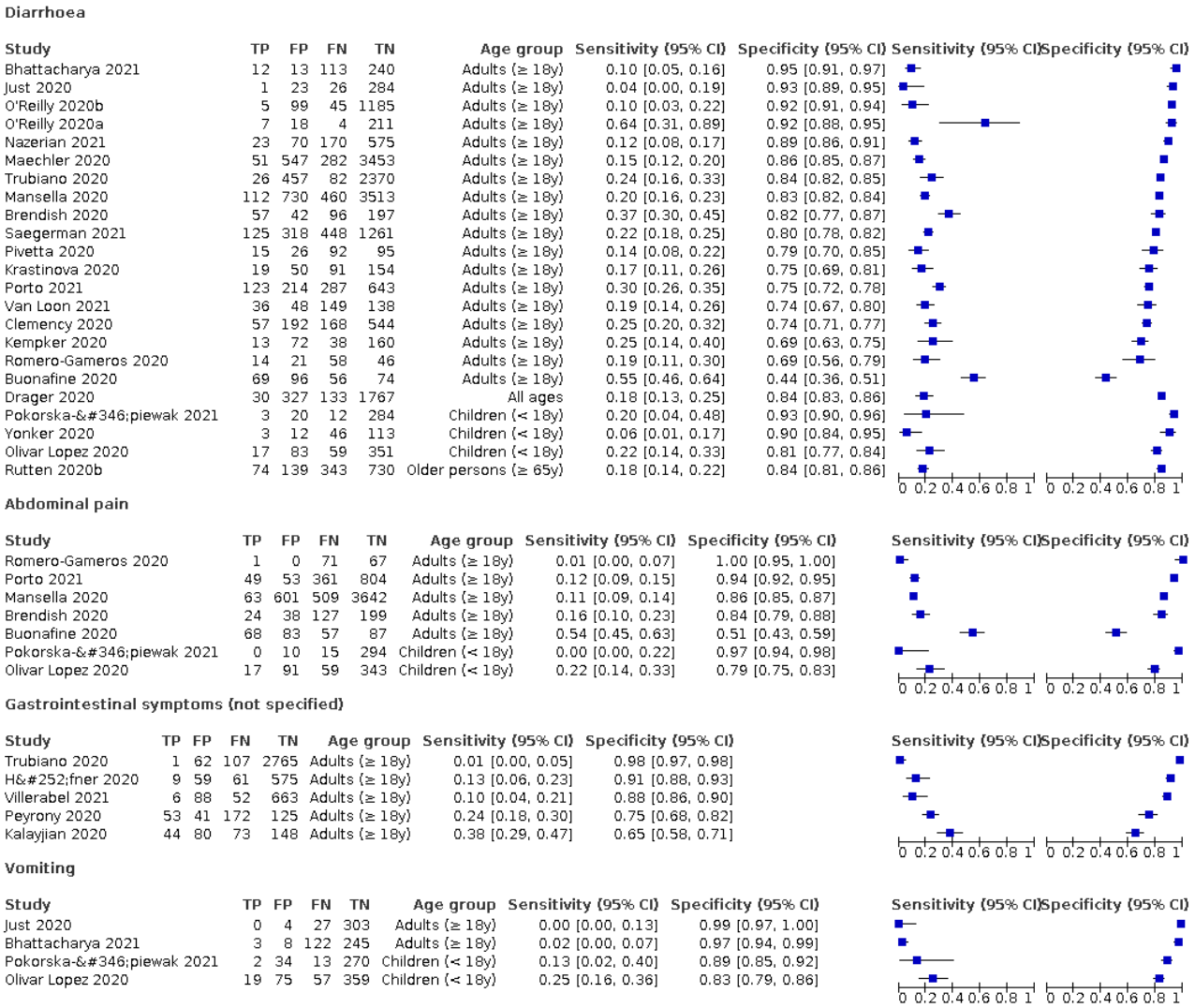


Figure 8. Forest plot of cardiovascular symptoms (palpitations)

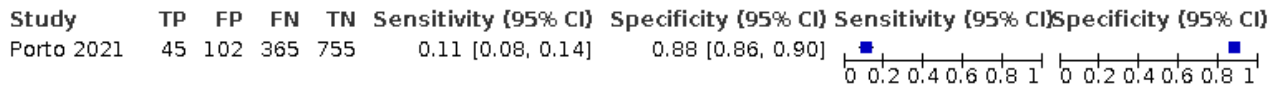


Figure 9. Forest plot of olfactory symptoms

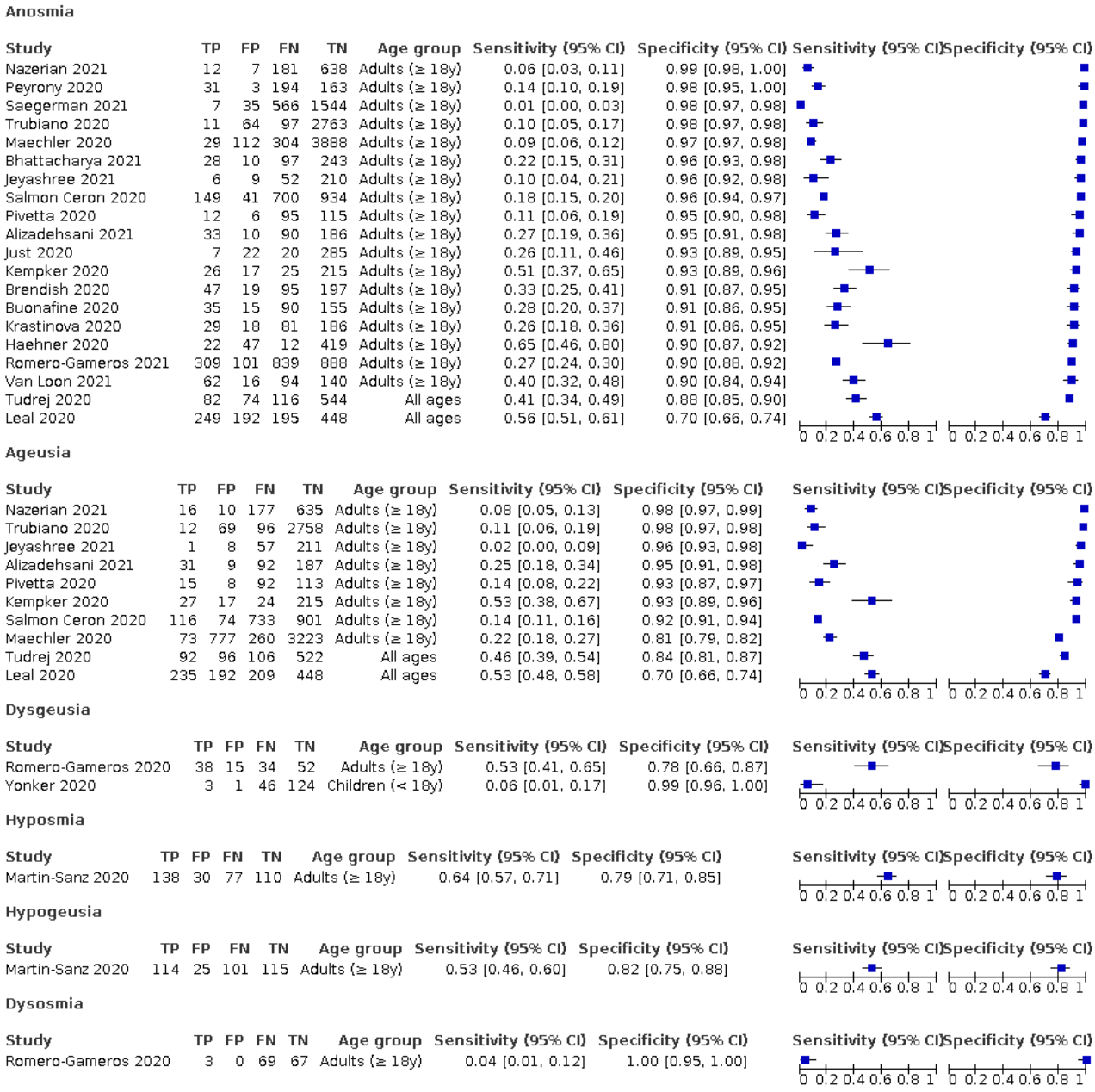
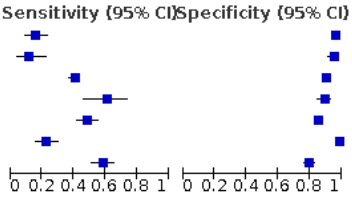


Figure 10. Forest plot of multivariable combinations of signs and symptoms

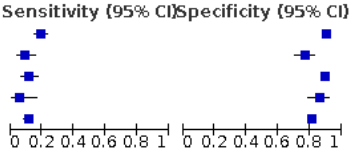
Anosmia or ageusia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	17	109	91	2718	Adults (≥ 18y)	0.16 [0.09, 0.24]	0.96 [0.95, 0.97]
Jeyashree 2021	7	11	51	208	Adults (≥ 18y)	0.12 [0.05, 0.23]	0.95 [0.91, 0.97]
Salmon Ceron 2020	346	95	503	880	Adults (≥ 18y)	0.41 [0.37, 0.44]	0.90 [0.88, 0.92]
Kempker 2020	31	24	20	208	Adults (≥ 18y)	0.61 [0.46, 0.74]	0.90 [0.85, 0.93]
Clemency 2020	110	108	115	628	Adults (≥ 18y)	0.49 [0.42, 0.56]	0.85 [0.83, 0.88]
Wee 2020	35	9	119	707	All ages	0.23 [0.16, 0.30]	0.99 [0.98, 0.99]
Tudrej 2020	116	126	82	492	All ages	0.59 [0.51, 0.66]	0.80 [0.76, 0.83]



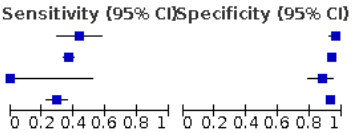
Nausea or vomiting

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	80	86	330	771	Adults (≥ 18y)	0.20 [0.16, 0.24]	0.90 [0.88, 0.92]
Krastinova 2020	10	47	100	157	Adults (≥ 18y)	0.09 [0.04, 0.16]	0.77 [0.71, 0.83]
Drager 2020	19	227	144	1867	All ages	0.12 [0.07, 0.18]	0.89 [0.88, 0.90]
Yonker 2020	3	17	46	108	Children (< 18y)	0.06 [0.01, 0.17]	0.86 [0.79, 0.92]
Rutten 2020b	48	163	369	706	Older persons (≥ 65y)	0.12 [0.09, 0.15]	0.81 [0.78, 0.84]



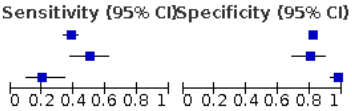
Anosmia and ageusia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Kempker 2020	22	10	29	222	Adults (≥ 18y)	0.43 [0.29, 0.58]	0.96 [0.92, 0.98]
Salmon Ceron 2020	314	66	535	909	Adults (≥ 18y)	0.37 [0.34, 0.40]	0.93 [0.91, 0.95]
Wernhart 2020	0	9	5	66	Adults (≥ 18y)	0.00 [0.00, 0.52]	0.88 [0.78, 0.94]
Tudrej 2020	58	44	140	574	All ages	0.29 [0.23, 0.36]	0.93 [0.91, 0.95]



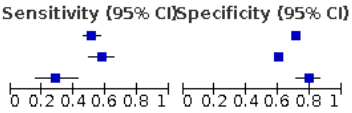
Anosmia or hyposmia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	157	154	253	703	Adults (≥ 18y)	0.38 [0.34, 0.43]	0.82 [0.79, 0.85]
Romero-Gameros 2020	36	13	36	54	Adults (≥ 18y)	0.50 [0.38, 0.62]	0.81 [0.69, 0.89]
Yonker 2020	10	3	39	122	Children (< 18y)	0.20 [0.10, 0.34]	0.98 [0.93, 1.00]



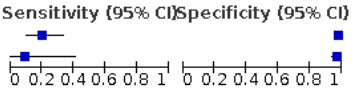
Myalgia or arthralgia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Maechler 2020	171	1145	162	2855	Adults (≥ 18y)	0.51 [0.46, 0.57]	0.71 [0.70, 0.73]
Drager 2020	94	827	69	1267	All ages	0.58 [0.50, 0.65]	0.61 [0.58, 0.63]
Yonker 2020	14	26	35	99	Children (< 18y)	0.29 [0.17, 0.43]	0.79 [0.71, 0.86]



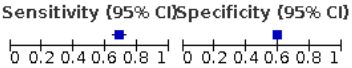
Anosmia or dysgeusia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
O'Reilly 2020b	10	32	40	1252	Adults (≥ 18y)	0.20 [0.10, 0.34]	0.98 [0.96, 0.98]
O'Reilly 2020a	1	7	10	222	Adults (≥ 18y)	0.09 [0.00, 0.41]	0.97 [0.94, 0.99]



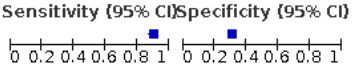
SCRiPS score, recent case detection rate

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	393	3469	178	5132	All ages	0.69 [0.65, 0.73]	0.60 [0.59, 0.61]



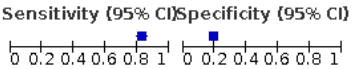
SCRIPS score, 0.5*recent case detection rate

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	514	5952	57	2649	All ages	0.90 [0.87, 0.92]	0.31 [0.30, 0.32]



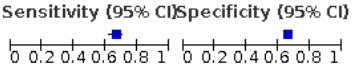
Cough or dyspnoea

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	473	6911	98	1690	All ages	0.83 [0.79, 0.86]	0.20 [0.19, 0.21]



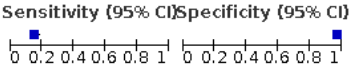
Multivariable score cut-off = 5

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Saegerman 2021	381	539	192	1040	Adults (≥ 18y)	0.66 [0.62, 0.70]	0.66 [0.63, 0.68]



Multivariable score cut-off = 8

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Saegerman 2021	89	53	484	1526	Adults (≥ 18y)	0.16 [0.13, 0.19]	0.97 [0.96, 0.97]



Cough and anosmia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	245	72	903	917	Adults (≥ 18y)	0.21 [0.19, 0.24]	0.93 [0.91, 0.94]

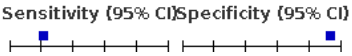


Figure 10. (Continued)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	245	72	903	917	Adults (≥ 18y)	0.21 [0.19, 0.24]	0.93 [0.91, 0.94]

Fever and anosmia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	188	43	960	946	Adults (≥ 18y)	0.16 [0.14, 0.19]	0.96 [0.94, 0.97]

Fever and cough and anosmia and dyspnoea and oxygen saturation < 93%

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	14	1	1134	988	Adults (≥ 18y)	0.01 [0.01, 0.02]	1.00 [0.99, 1.00]

Fever and dyspnoea

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	385	118	763	871	Adults (≥ 18y)	0.34 [0.31, 0.36]	0.88 [0.86, 0.90]

Anosmia and dyspnoea

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	155	43	993	946	Adults (≥ 18y)	0.14 [0.12, 0.16]	0.96 [0.94, 0.97]

Fever and cough

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	515	153	633	836	Adults (≥ 18y)	0.45 [0.42, 0.48]	0.85 [0.82, 0.87]

Weakness or fatigue

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	152	272	258	585	Adults (≥ 18y)	0.37 [0.32, 0.42]	0.68 [0.65, 0.71]

Hyposmia or anosmia

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Villerabel 2021	18	20	40	731	Adults (≥ 18y)	0.31 [0.20, 0.45]	0.97 [0.96, 0.98]

Diarrhoea and nausea

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	0	3	175	420	Adults (≥ 18y)	0.00 [0.00, 0.02]	0.99 [0.98, 1.00]

Myalgia and asthenia and fever

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	81	162	94	261	Adults (≥ 18y)	0.46 [0.39, 0.54]	0.62 [0.57, 0.66]

Cough and fever and sputum production

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	37	81	138	342	Adults (≥ 18y)	0.21 [0.15, 0.28]	0.81 [0.77, 0.84]

Cough and fever and sputum production and dyspnoea

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	21	27	154	396	Adults (≥ 18y)	0.12 [0.08, 0.18]	0.94 [0.91, 0.96]

Dyspnoea and cough and fever and low oxygen saturation

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	5	9	170	414	Adults (≥ 18y)	0.03 [0.01, 0.07]	0.98 [0.96, 0.99]

Sore throat and nasal congestion and sneezing and mild fever

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	18	109	157	314	Adults (≥ 18y)	0.10 [0.06, 0.16]	0.74 [0.70, 0.78]

Rhinitis or pharyngitis

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	19	26	206	140	Adults (≥ 18y)	0.08 [0.05, 0.13]	0.84 [0.78, 0.90]

Dizziness or syncope

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	8	13	217	153	Adults (≥ 18y)	0.04 [0.02, 0.07]	0.92 [0.87, 0.96]

Figure 10. (Continued)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	8	13	217	153	Adults (≥ 18y)	0.04 [0.02, 0.07]	0.92 [0.87, 0.96]

CSBSS (cut-off = 41.7)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	81	96	44	157	Adults (≥ 18y)	0.65 [0.56, 0.73]	0.62 [0.56, 0.68]

Myalgia and fatigue

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wernhart 2020	3	50	2	25	Adults (≥ 18y)	0.60 [0.15, 0.95]	0.33 [0.23, 0.45]

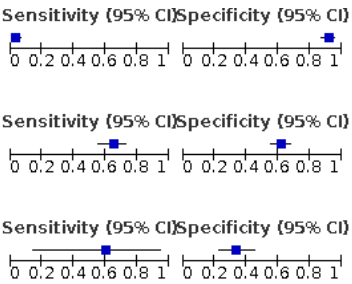


Figure 11. Summary ROC plot of upper respiratory tract symptoms. The study points (symbols) were scaled according to the sample size

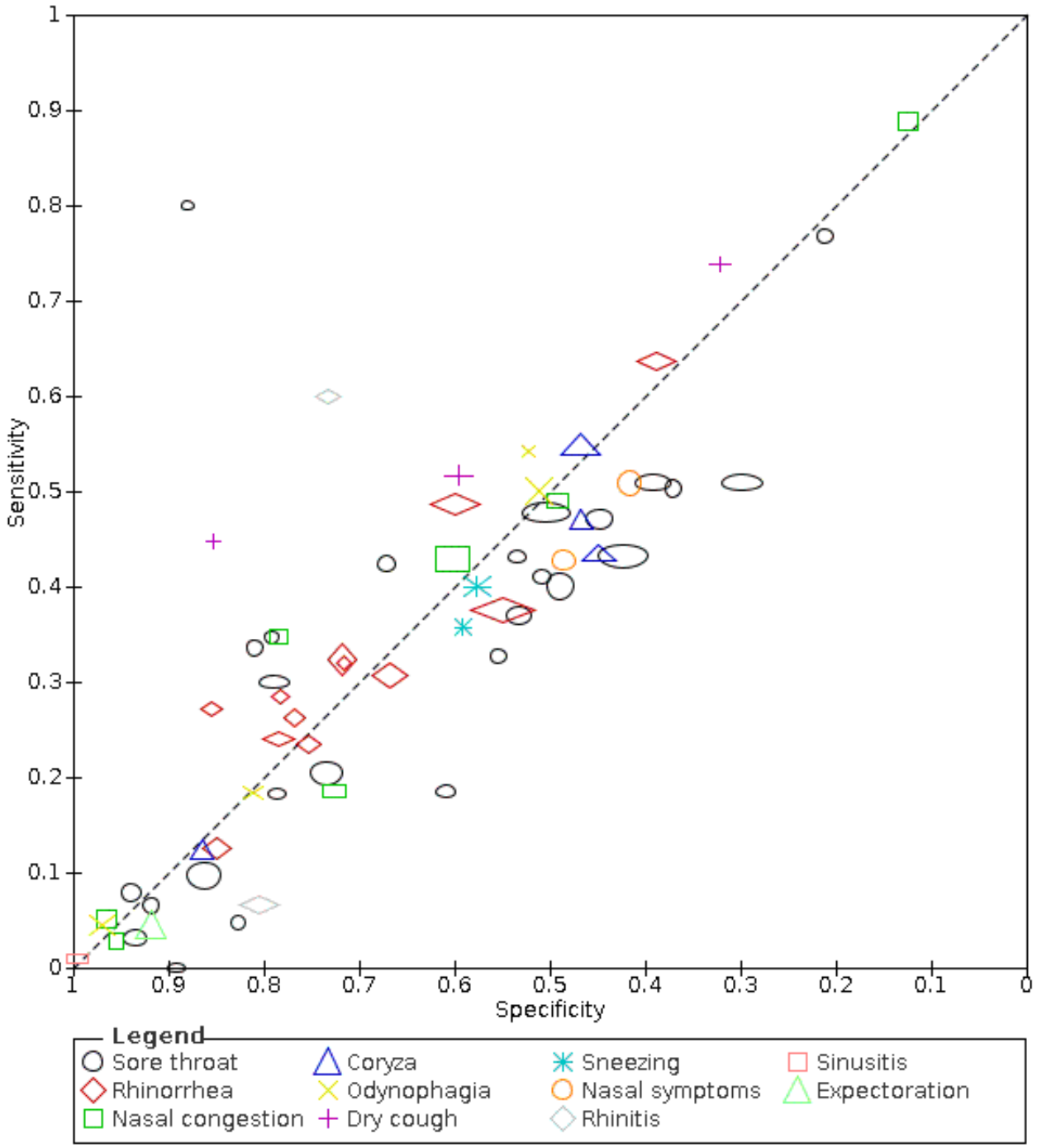


Figure 12. Summary ROC plot of lower respiratory tract symptoms. The study points (symbols) were scaled according to the sample size

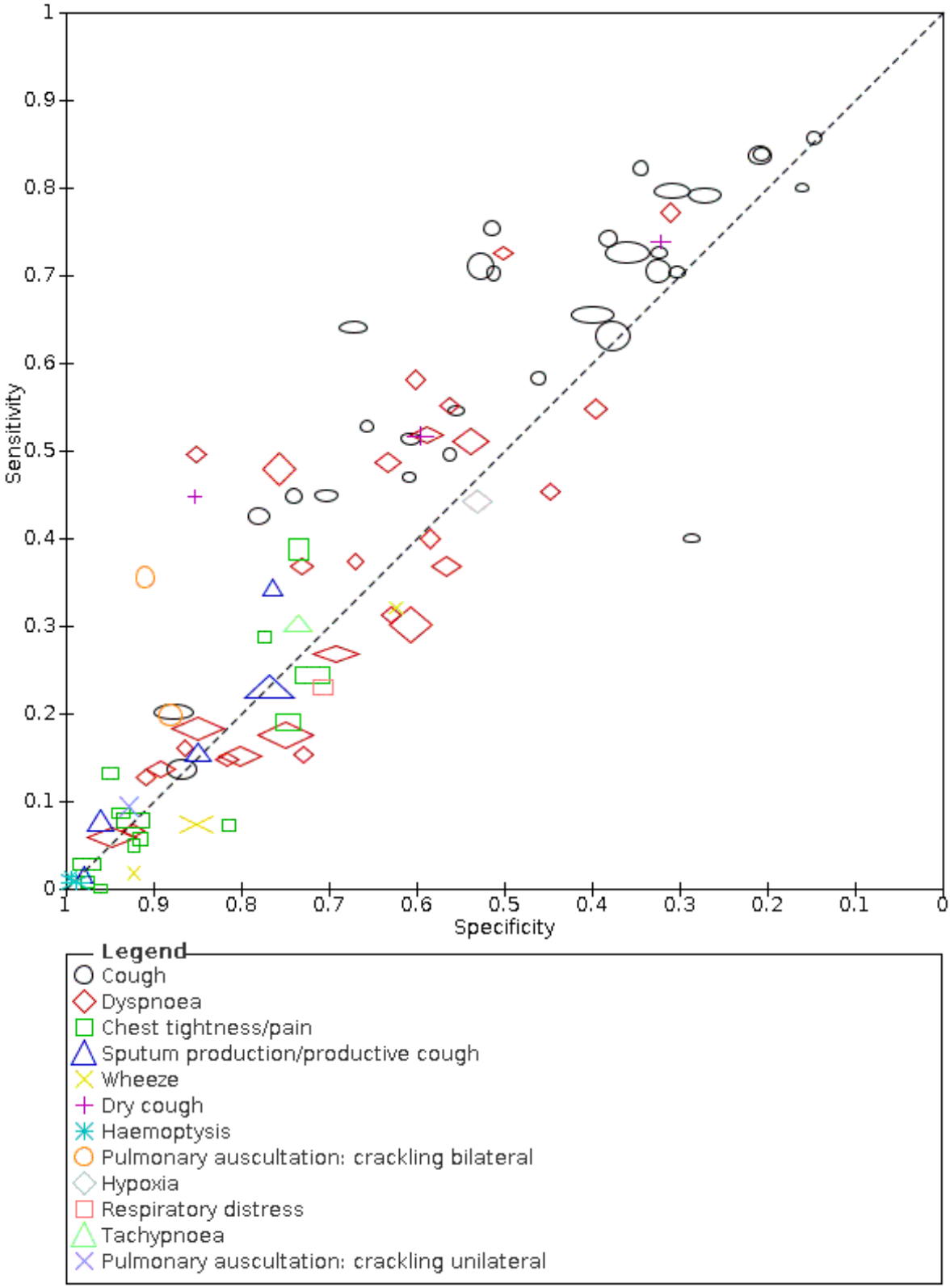


Figure 13. Summary ROC plot of systemic signs and symptoms. The study points (symbols) were scaled according to the sample size

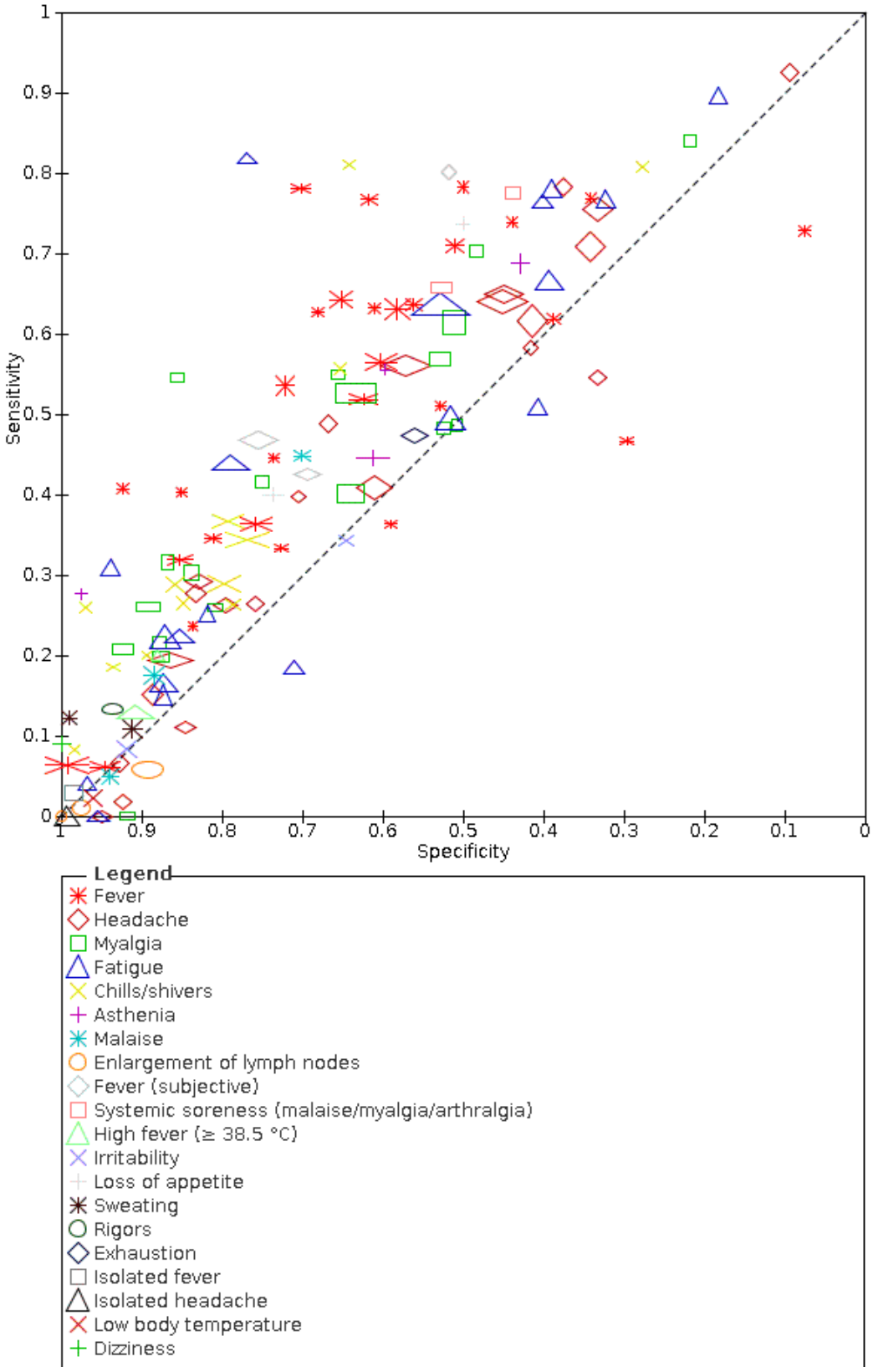


Figure 13. (Continued)

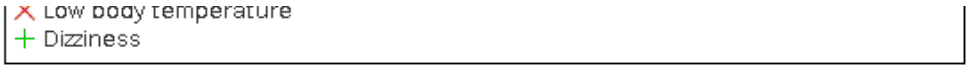


Figure 14. Summary ROC plot of gastrointestinal symptoms. The study points (symbols) were scaled according to the sample size

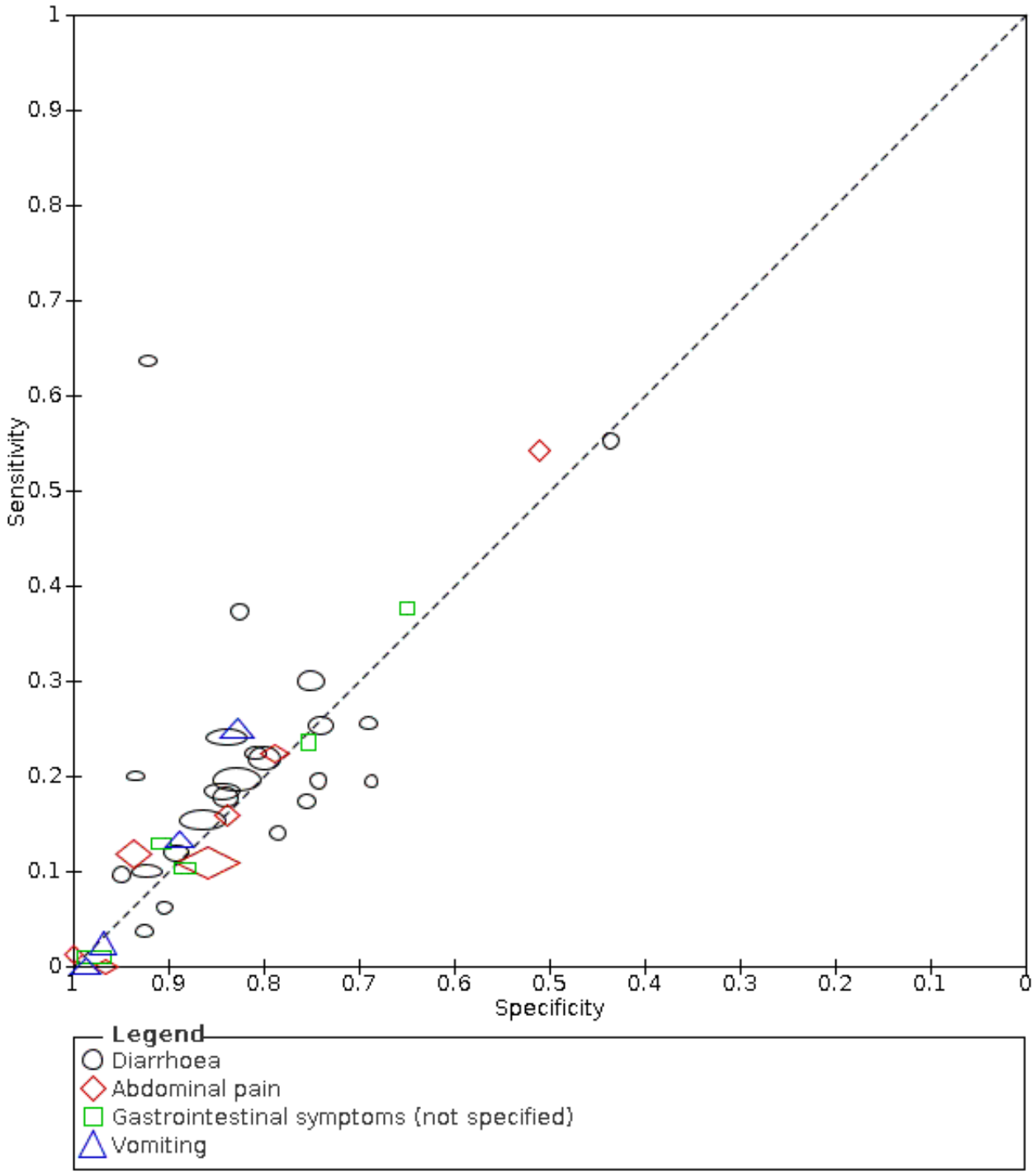


Figure 15. Summary ROC plot of olfactory symptoms. The study points (symbols) were scaled according to the sample size

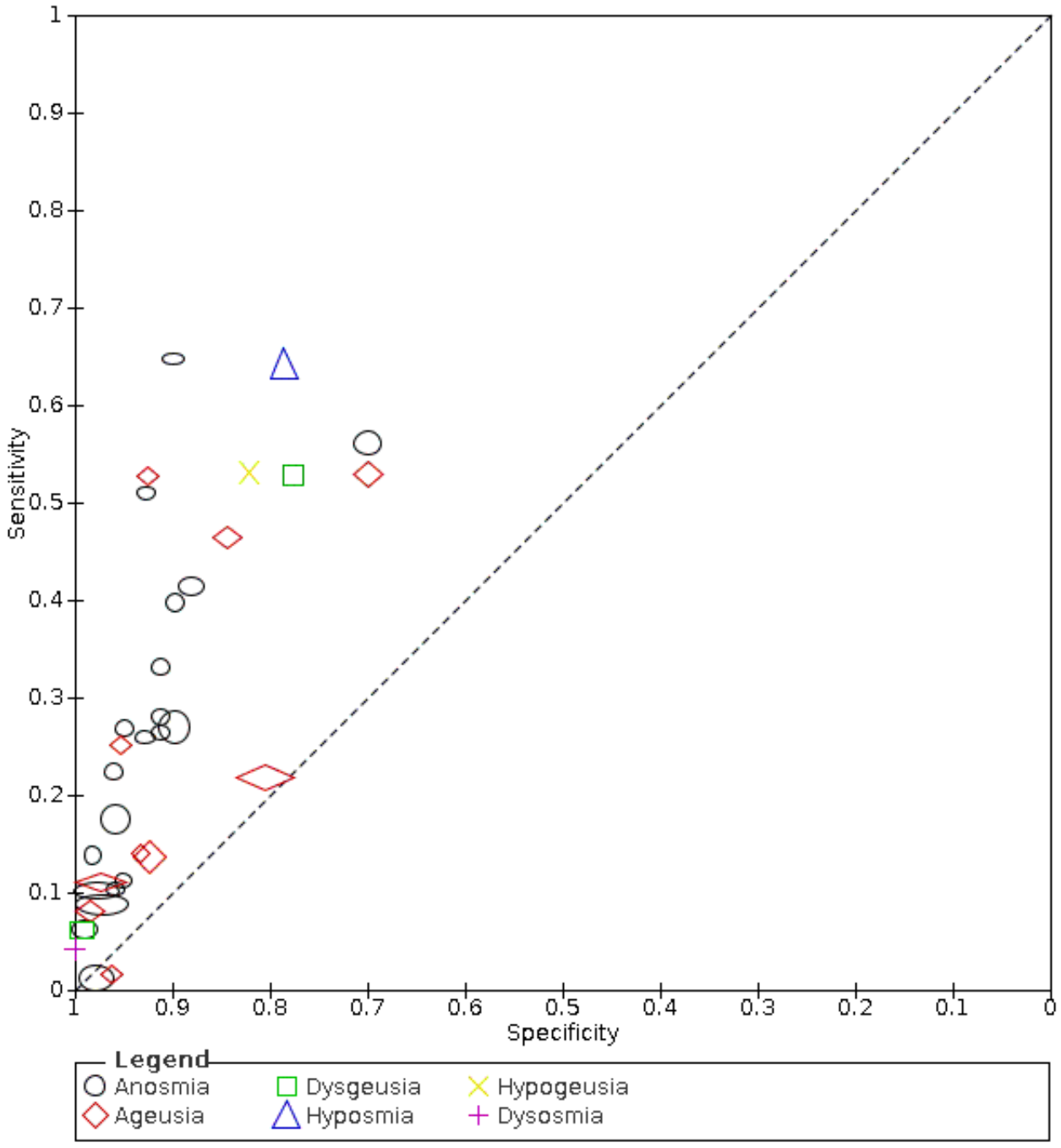


Figure 16. Summary ROC plot of multivariable combinations of signs and symptoms. The study points (symbols) were scaled according to the sample size

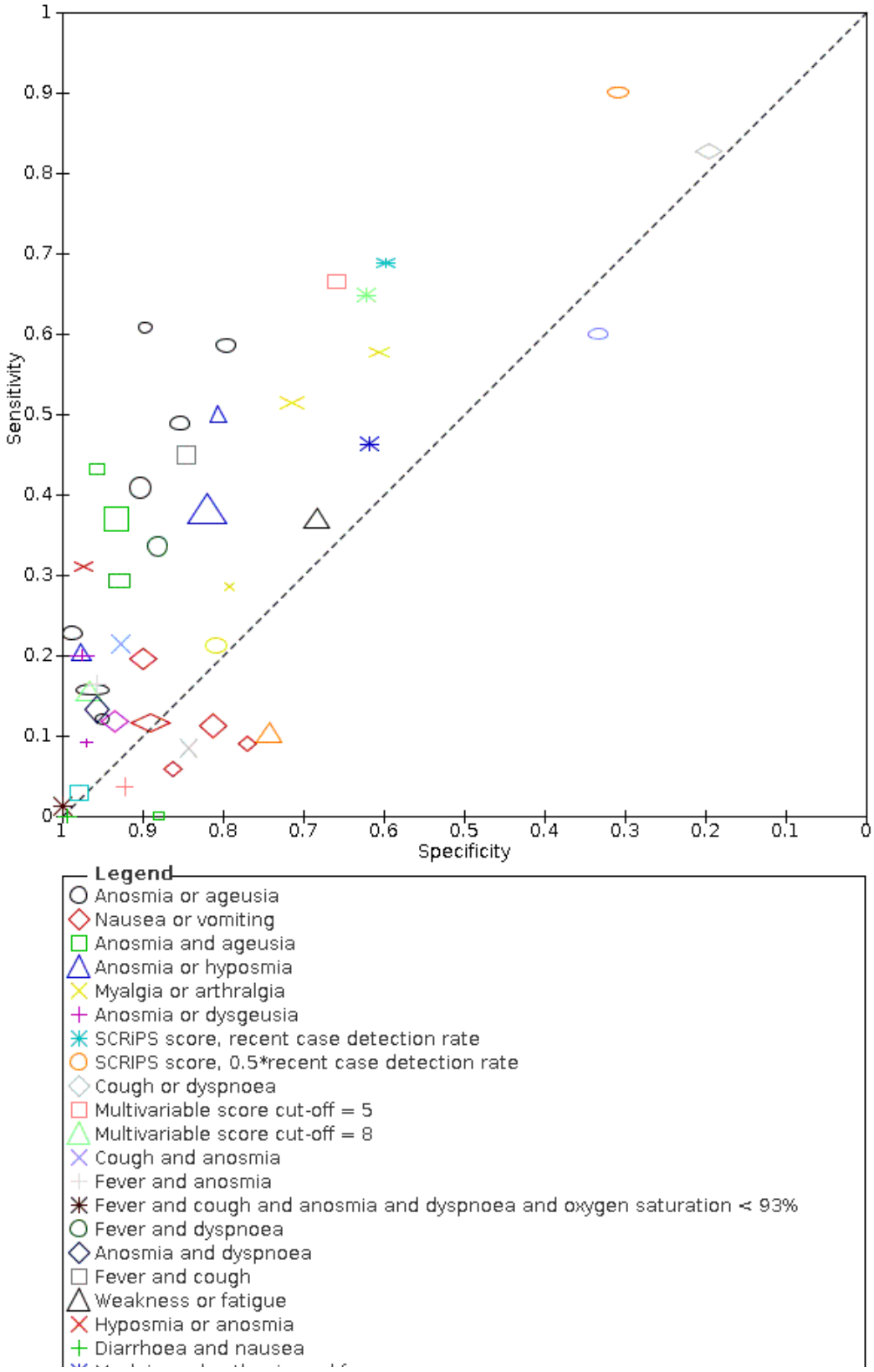


Figure 16. (Continued)

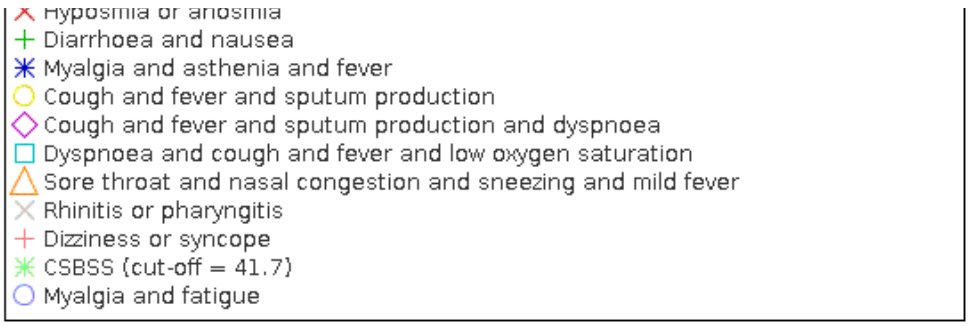


Figure 17. Summary ROC plot of fever by risk of bias concerning participant selection. Summary points and their 95% confidence regions are shown for high and low risk of bias only. The study points (symbols) were scaled according to the sample size

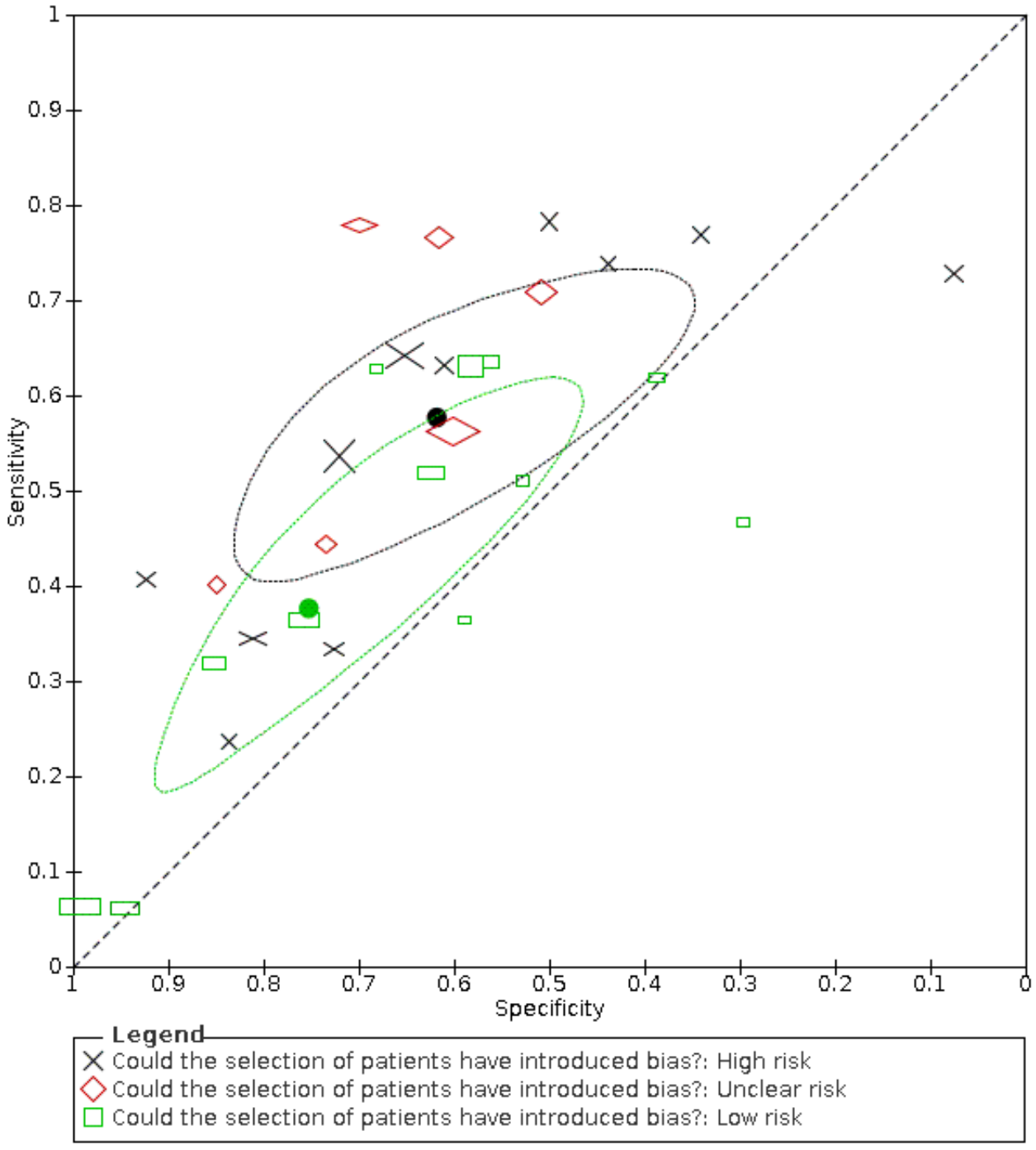


Figure 18. Summary ROC plot of cough by risk of bias concerning participant selection. Summary points and their 95% confidence regions are shown for high and low risk of bias only. The study points (symbols) were scaled according to the sample size

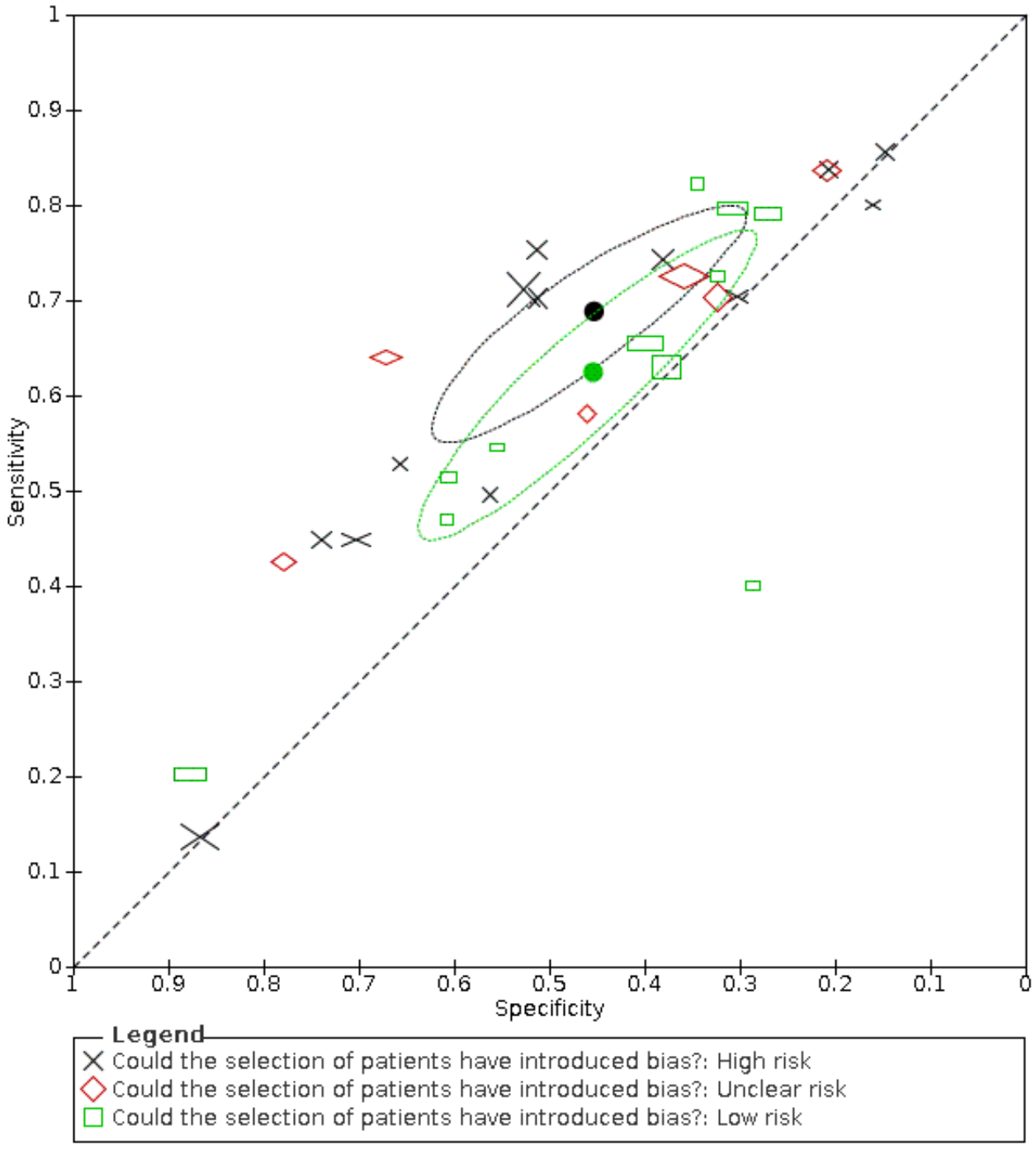
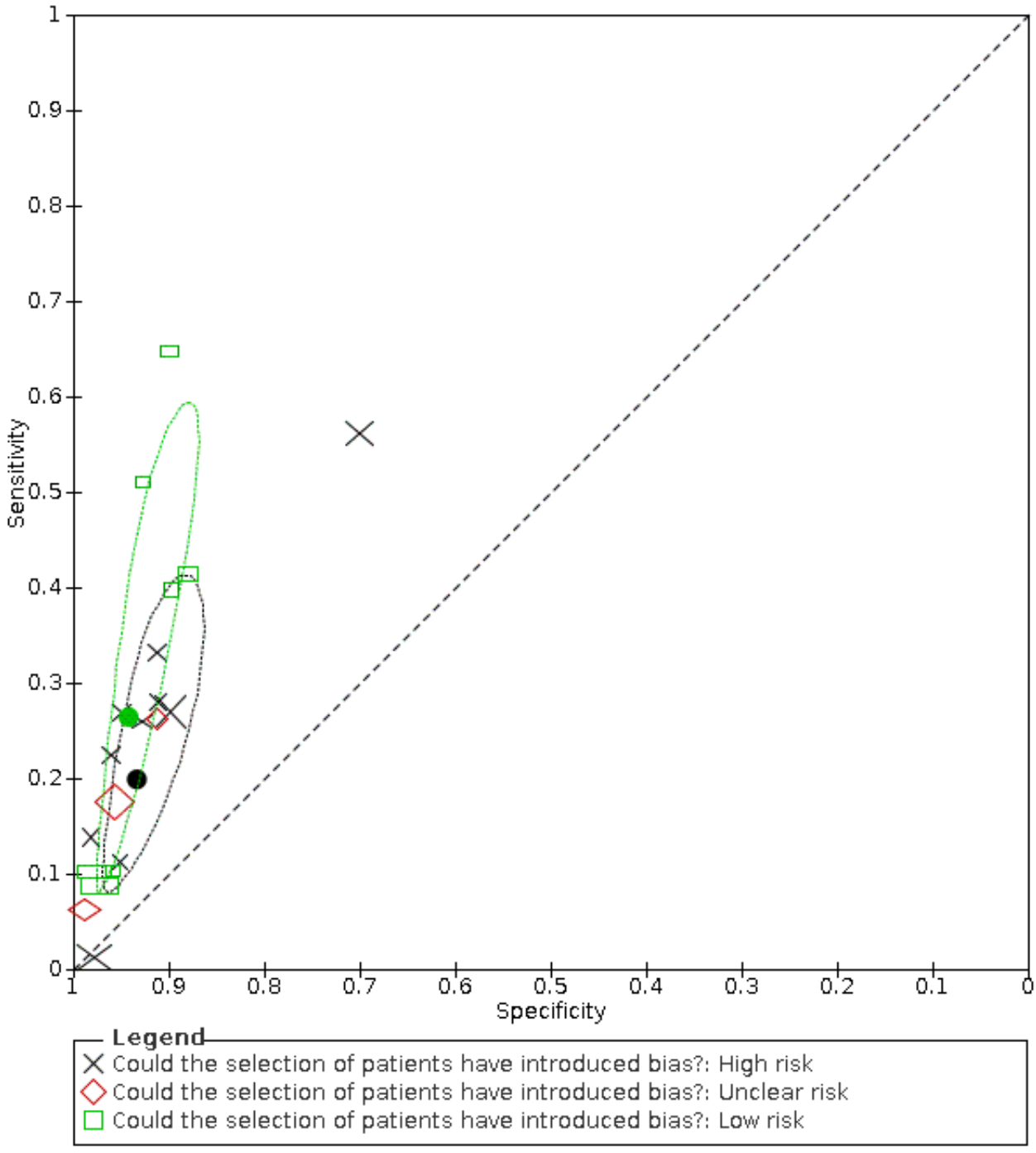


Figure 19. Summary ROC plot of anosmia by risk of bias concerning participant selection. Summary points and their 95% confidence regions are shown for high and low risk of bias only. The study points (symbols) were scaled according to the sample size



Summary results

We conducted meta-analyses for 13 symptoms at presentation (fever, dyspnoea, cough, diarrhoea, sore throat, fatigue, rhinorrhoea, headache, anosmia, anosmia or ageusia, ageusia, myalgia, chills/shivers). The ranges and summary estimates of the sensitivity and specificity of the 13 index tests are listed below, ordered by decreasing number of studies included. Summary estimates of test accuracy are listed in additional Table 3. They are based on bivariate meta-analyses of prospective studies with low risk of bias for participant selection.

- Fever, 12 studies, 28,495 participants: sensitivity range 6% to 64% (summary 37.6%, 95% CI 23.4% to 54.3%); specificity range 30% to 99% (summary 75.2%, 95% CI 56.3% to 87.8%)
- Dyspnoea, 12 studies, 19,545 participants: sensitivity range 6% to 73% (summary 23.3%, 95% CI 16.4% to 31.9%); specificity range 50% to 95% (summary 75.7%, 95% CI 65.2% to 83.9%)
- Cough, 11 studies, 18,702 participants: sensitivity range 20% to 82% (summary 62.4%, 95% CI 50.6% to 72.9%); specificity range 27% to 88% (summary 45.4%, 95% CI 33.5% to 57.9%)
- Diarrhoea, 11 studies, 13,669 participants: sensitivity range 6% to 64% (summary 18.5%, 95% CI 15.7% to 21.6%); specificity range 69% to 93% (summary 84.1%, 95% CI 79.4% to 87.9%)
- Sore throat, 10 studies, 14,548 participants: sensitivity range 0% to 51% (summary 31.0%, 95% CI 20.2% to 44.5%); specificity range 30% to 89% (summary 61.9%, 95% CI 46.7% to 75.0%)
- Fatigue, eight studies, 7967 participants: sensitivity range 0% to 82% (summary 40.2%, 95% CI 19.4% to 65.1%); specificity range 32% to 97% (summary 73.6%, 95% CI 48.4% to 89.3%)
- Rhinorrhoea, seven studies, 17,972 participants: sensitivity range 12% to 64% (summary 30.3%, 95% CI 18.7% to 45.1%); specificity range 39% to 86% (summary 70.0%, 95% CI 56.8% to 80.6%)
- Headache, seven studies, 10,899 participants: sensitivity range 0% to 78% (summary 35.8%, 95% CI 17.2% to 60.0%); specificity range 38% to 95% (summary 73.0%, 95% CI 53.4% to 86.4%)
- Anosmia, seven studies, 9456 participants: sensitivity range 9% to 65% (summary 26.4%, 95% CI 13.8% to 44.6%); specificity range 88% to 98% (summary 94.2%, 95% CI 90.6% to 96.5%)
- Anosmia or ageusia, six studies, 6142 participants: sensitivity range 12% to 61% (summary 39.2%, 95% CI 26.5% to 53.6%); specificity range 80% to 99% (summary 92.1%, 95% CI 84.5% to 96.2%)
- Myalgia, six studies, 2684 participants: sensitivity range 0% to 70% (summary 37.5%, 95% CI 20.6% to 58.1%); specificity range 48% to 92% (summary 75.4%, 95% CI 58.4% to 87.0%)
- Chills/shivers, five studies, 14,472 participants: sensitivity range 8% to 81% (summary 25.3%, 95% CI 15.1% to 39.3%); specificity range 64% to 98% (summary 85.0%, 95% CI 72.1% to 92.6%)
- Ageusia, five studies, 8644 participants: sensitivity range 2% to 53% (summary 23.2%, 95% CI 10.6% to 43.3%); specificity range 81% to 98% (summary 92.6%, 95% CI 83.1% to 97.0%)

Cough was the only index test with a summary sensitivity above 50%. Its summary specificity was 45.4% (Table 3). Summary specificity was above 90% for anosmia, ageusia and for the presence of anosmia or ageusia (Table 3). However, their summary sensitivity was low (maximum 39.2% for anosmia or ageusia).

The summary positive likelihood ratios (LRs+) of anosmia as a single test or in combination with ageusia ('anosmia or ageusia') was just below our predefined cut-off of 5 for a useful red flag (4.55, 95% CI 3.46 to 5.97) and 4.99, 95% CI 3.22 to 7.75) respectively). The summary negative likelihood ratios (LRs-) were too high to make any of the reported tests useful for ruling out COVID-19. In other words, the absence of the above-mentioned symptoms or signs does not necessarily imply the absence of COVID-19.

Combinations of signs and symptoms

Twenty-four studies assessed combinations of different signs and symptoms (Figure 10; Figure 16). In total, 29 different combinations were assessed, of which only six were assessed by more than one study.

Three multivariable prediction scores were reported (Bhattacharya 2021; Saegerman 2021; Van Walraven 2021). Bhattacharya 2021 (378 participants) used a combination of only signs and symptoms (Clinical Symptom-Based Scoring System (CSBSS) based on body temperature, cough, headache, myalgia and anosmia), leading to a sensitivity of 64.8% (95% CI 55.8% to 73.1%) and a specificity of 62.1% (95% CI 55.8% to 68.1%) at the proposed cut-off of 41.7 points. Reducing the cut-off to 10 points led to a sensitivity of 75.0% and a specificity of 42.6%. The Area Under the ROC Curve (AUC) was 0.69 (95% CI 0.62 to 0.76) for the validation dataset.

The other two multivariable prediction score studies combined signs and symptoms with other information: Saegerman 2021 (2152 participants) combined age (> 56.5 years) with the presence of chest pain, sore throat, dry cough or fever, leading to a sensitivity of 66.5% (95% CI 62.5% to 70.4%) and a specificity of 65.9% (95% CI 63.5% to 68.2%) at the lowest cut-off. The AUC of this score was 0.71 (95% CI 0.69 to 0.73). Van Walraven 2021 (9172 participants) developed a score, based on a combination of gender, being a healthcare worker, recent contact with a COVID-19 case, recent travel, the recent local case detection rate, the presence of rhinorrhoea, cough or dyspnoea, and a combination of age and the presence of fever (SARS-CoV-2 Risk Prediction Score (SCRiPS)). The recent local case detection rate was calculated as the proportion of tests from the testing clinic in the previous three days that were SARS-CoV-2-positive. The SCRiPS score using 0.5 times the recent local case detection rate demonstrated the highest sensitivity of all combinations (90.0%; 95% CI 87.3% to 92.4%) at the cost of lower specificity (30.8%, 95% CI 29.8% to 31.8%). The second highest sensitivity was reported by the same study (Van Walraven 2021), using only the presence of cough or dyspnoea. This combination led to a sensitivity of 82.8% (95% CI 79.5% to 85.8%) at a specificity of 19.6% (95% CI 18.8% to 20.5%).

In addition to anosmia or ageusia (see pooled results), some other paired combinations of symptoms were investigated (Figure 10; Figure 16). The following combinations showed a sensitivity of more than 50% in at least one study.

- Anosmia or hyposmia (3 studies): sensitivity from 20% to 50% and specificity from 81% to 98%
- Myalgia or arthralgia (3 studies): sensitivity from 29% to 58% and specificity from 61% to 79%
- Cough or dyspnoea (1 study): sensitivity of 83%, specificity of 20%
- Myalgia and fatigue (1 study): sensitivity of 60%, specificity of 33%

Positivity rates

Positivity rates (presence of the symptom in the study population) of signs and symptoms depend on prevalence of COVID-19 and population characteristics, especially preselection. As a result, positivity rates were highly variable. In studies with prevalence less than 10%, suggesting little preselection had taken place, positivity rates for fever were between 1.2% and 69.3% (24.7% average), for cough between 12.7% and 83.7% (54.9% average), for anosmia between 2.5% and 13.8% (7.1% average), for ageusia (2 studies) between 2.8% and 19.6% (11.2% average), and for anosmia or ageusia (1 study) 4.3%.

Stratified analyses

Stratification by age group

Three prospective studies were performed specifically in children (Olivar Lopez 2020; Pokorska-Śpiewak 2021; Yonker 2020), and two overlapping studies in older people living in a nursing home (Rutten 2020a; Rutten 2020b). All other studies were either performed in adults or in individuals of all ages. Meta-analysis of data in children or older adults was impossible due to the limited number of studies in these age groups. We therefore limited ourselves to descriptive analyses. All forest plots (Figure 4; Figure 5; Figure 6; Figure 7; Figure 8; Figure 9; Figure 10) and Dumbbell plots (Figure 20; Figure 21; Figure 22) are ordered by age group (adults, all ages, children, older adults (≥ 65 years)).

Figure 20. Dumbbell plot: olfactory symptoms

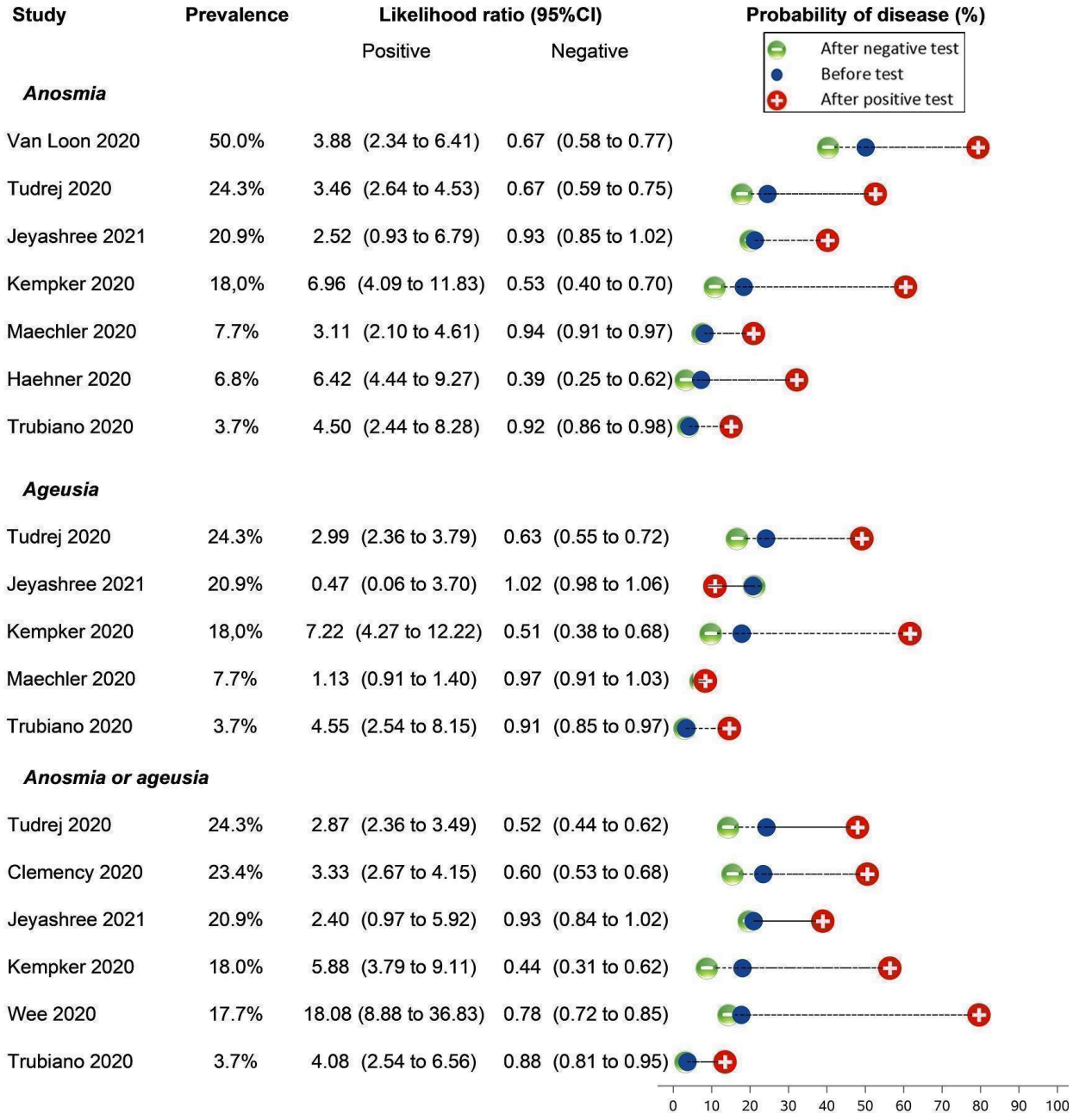


Figure 21. Dumbbell: plot fever. Ordered by age group - children (< 18 years), adults/all ages, older adults (≥ 65 years)

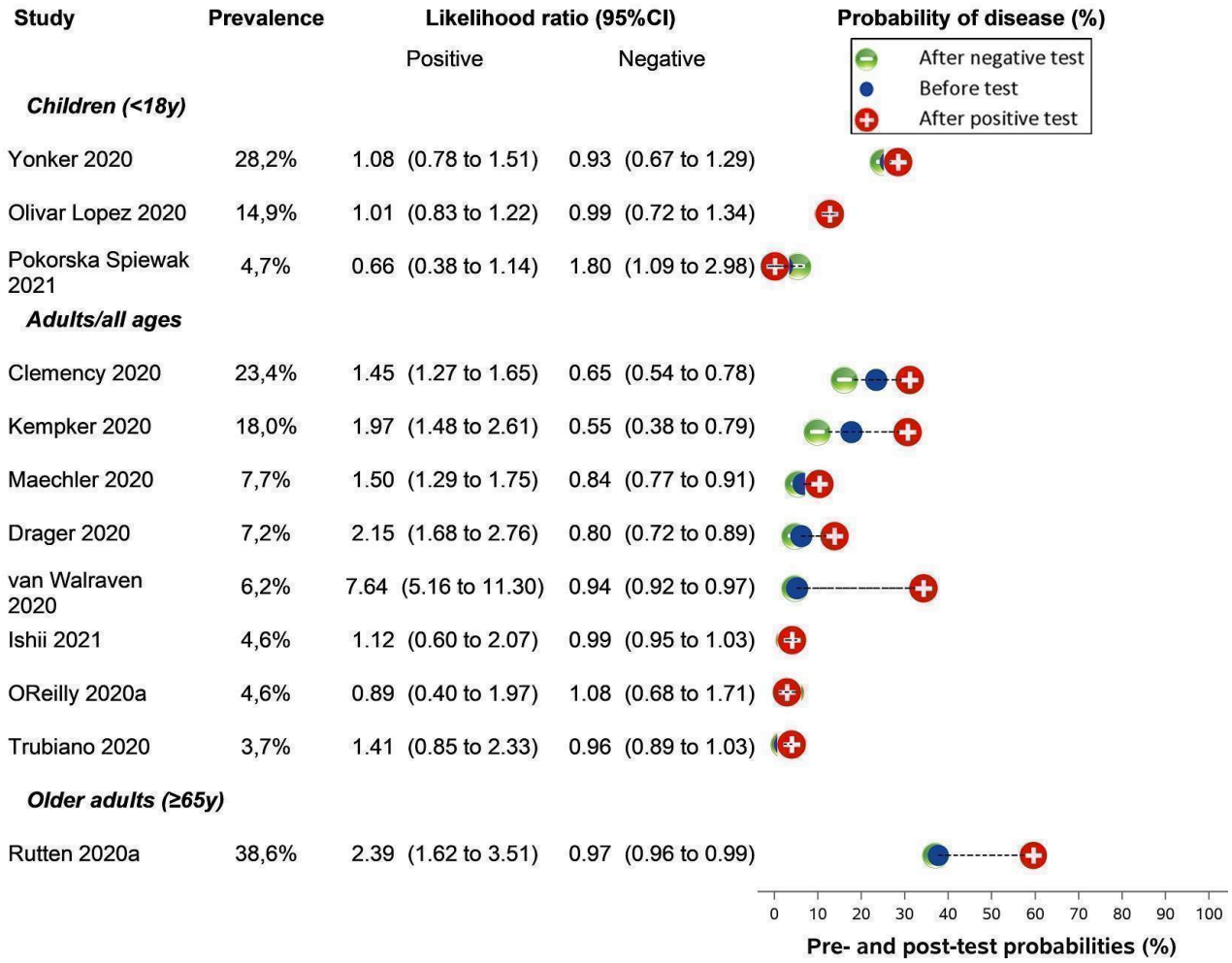
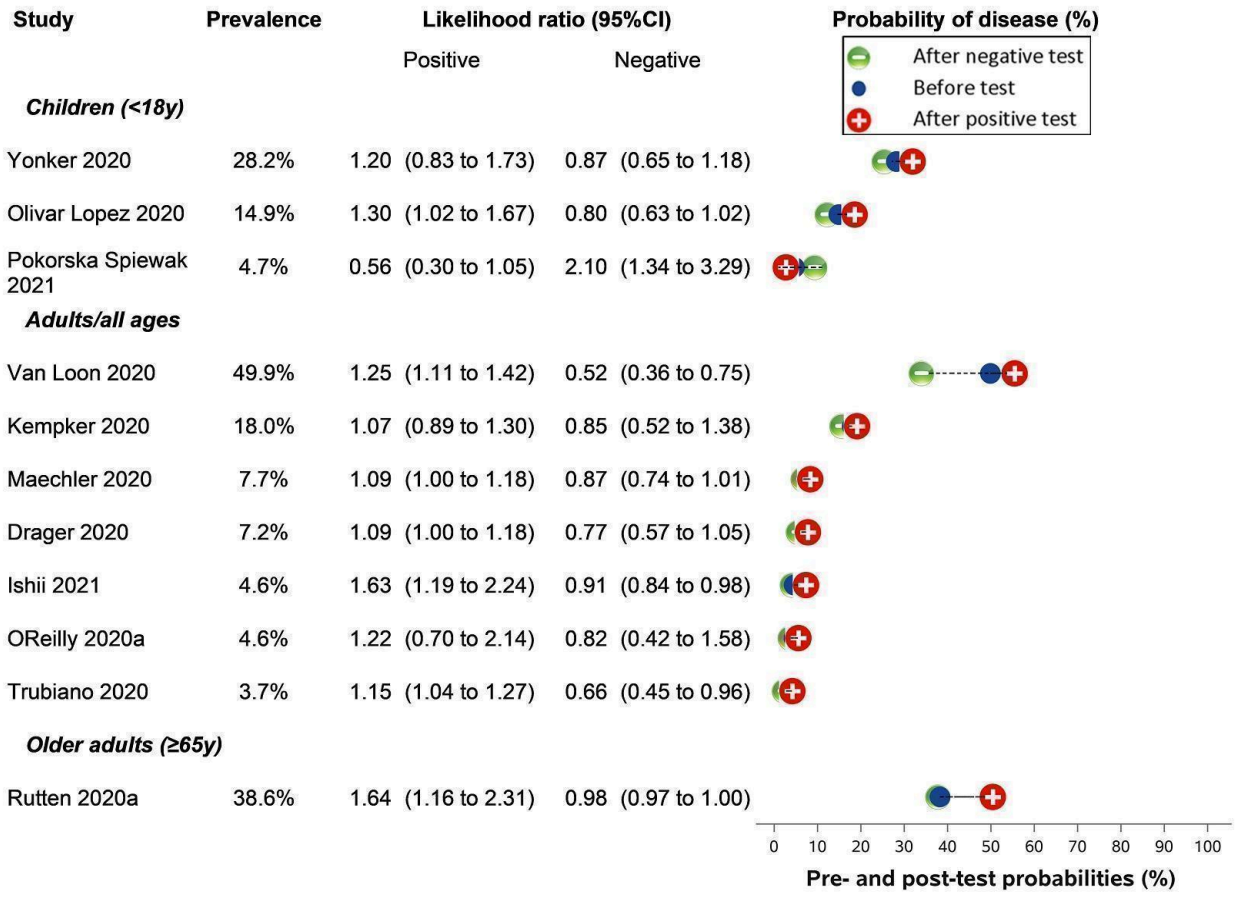


Figure 22. Dumbbell plot: cough. Ordered by age group - children (< 18 years), adults/all ages, older adults (≥ 65 years)



In children, compared to the adult population, the differences in diagnostic accuracy depended strongly on the type of symptom. For example, the sensitivity of fever in children ranged from 47% to 62%, which is higher than the overall summary result for all ages (29%). The specificity of fever in children ranged from 30% to 53%, which is lower than the overall summary result (82.2%). In contrast, we observed lower sensitivity and higher specificity for fatigue, headache and myalgia in children than in the population as a whole.

The results for sore throat, rhinorrhoea, cough, dyspnoea and diarrhoea were comparable with the overall population. Olfactory symptoms were rarely investigated in children. One study (Yonker 2020), investigated the diagnostic value of dysgeusia, observing similar accuracy to in the adult population.

In older adults living in a nursing home, most symptoms showed sensitivities and specificities that were comparable to the overall summary results (Rutten 2020b). The sensitivity of fever appeared to be higher in older people, but this may be due to a strong preselection based on the presence of fever.

Stratification according to risk of bias in patient selection

The summary estimates of fever, cough and anosmia from prospective studies that had either a low or a high risk of bias concerning participant selection are presented in ROC curves for comparison (Figure 17; Figure 18; Figure 19). We observed the largest difference between both summary estimates for fever. The differences between the summary estimates between low and high risk of bias concerning participant selection were less pronounced for cough and for anosmia.

Stratification by care setting

Stratification according to setting did not explain the observed heterogeneity in diagnostic accuracy.

Additional analyses

To further illustrate the ability of a test to either rule in or rule out COVID-19, we constructed dumbbell plots showing pre- and post-test probabilities for anosmia, anosmia or ageusia, fever and cough by age group in each prospective cross-sectional study with a low risk of bias rating for selection of participants (Haehner 2020; Jeyashree 2021; Kempker 2020; Maechler 2020; Trubiano

2020; Tudrej 2020; Van Loon 2021; see Figure 20; Figure 21; Figure 22). For each test, we have plotted the pre-test probability, which is the prevalence of COVID-19 disease in the study (blue dot). The probability of having COVID-19 disease after testing (post-test probability) then changes depending on a positive test result (red dot marked +) or a negative test result (green dot marked -). The plot shows that the presence of anosmia, for example, increased the probability of COVID-19 in all seven studies. Its absence slightly decreased the probability of COVID-19 in three studies (Kempker 2020; Tudrej 2020; Van Loon 2021), and in the four other studies there was not much difference between pre- and post-test probability (Haehner 2020; Jeyashree 2021; Maechler 2020; Trubiano 2020).

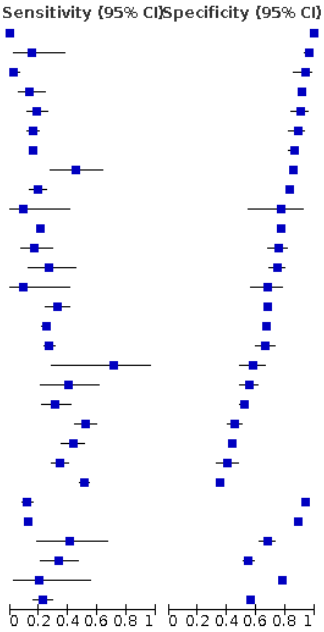
Findings: retrospective studies

Results of retrospective studies are presented in forest plots (Figure 23; Figure 24; Figure 25; Figure 26; Figure 27; Figure 28; Figure 29).

Figure 23. Forest plot of upper respiratory signs/symptoms (retrospective data collection)

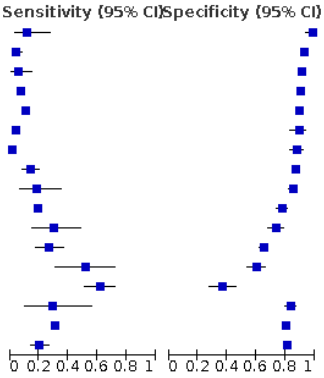
Sore throat (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	1	3	627	305	Adults (≥ 18y)	0.00 [0.00, 0.01]	0.99 [0.97, 1.00]
Haliga 2021	3	9	17	224	Adults (≥ 18y)	0.15 [0.03, 0.38]	0.96 [0.93, 0.98]
Langer 2020	3	5	121	70	Adults (≥ 18y)	0.02 [0.01, 0.07]	0.93 [0.85, 0.98]
Hüfner 2020	9	60	56	610	Adults (≥ 18y)	0.14 [0.07, 0.25]	0.91 [0.89, 0.93]
Arslan 2021	25	11	110	103	Adults (≥ 18y)	0.19 [0.12, 0.26]	0.90 [0.83, 0.95]
Huang 2020	54	16	282	123	Adults (≥ 18y)	0.16 [0.12, 0.20]	0.88 [0.82, 0.93]
King 2020	311	67	1676	409	Adults (≥ 18y)	0.16 [0.14, 0.17]	0.86 [0.82, 0.89]
Chew 2021	15	103	18	602	Adults (≥ 18y)	0.45 [0.28, 0.64]	0.85 [0.83, 0.88]
Mao 2020	36	140	152	676	Adults (≥ 18y)	0.19 [0.14, 0.26]	0.83 [0.80, 0.85]
Cheng 2020	1	5	10	17	Adults (≥ 18y)	0.09 [0.00, 0.41]	0.77 [0.55, 0.92]
Nitecki 2021	284	5272	1054	17752	Adults (≥ 18y)	0.21 [0.19, 0.24]	0.77 [0.77, 0.78]
Kim 2020	9	47	45	141	Adults (≥ 18y)	0.17 [0.08, 0.29]	0.75 [0.68, 0.81]
Shah 2020	9	73	24	210	Adults (≥ 18y)	0.27 [0.13, 0.46]	0.74 [0.69, 0.79]
Peng 2020	1	24	10	51	Adults (≥ 18y)	0.09 [0.00, 0.41]	0.68 [0.56, 0.78]
Ahmed 2021	40	545	83	1153	Adults (≥ 18y)	0.33 [0.24, 0.42]	0.68 [0.66, 0.70]
Barbhaya 2021	210	532	636	1093	Adults (≥ 18y)	0.25 [0.22, 0.28]	0.67 [0.65, 0.70]
Chan 2021	139	71	371	140	Adults (≥ 18y)	0.27 [0.23, 0.31]	0.66 [0.60, 0.73]
Feng 2021	5	53	2	72	Adults (≥ 18y)	0.71 [0.29, 0.96]	0.58 [0.48, 0.66]
Ide 2021	10	113	15	139	Adults (≥ 18y)	0.40 [0.21, 0.61]	0.55 [0.49, 0.61]
Leung 2021	27	563	59	609	Adults (≥ 18y)	0.31 [0.22, 0.42]	0.52 [0.49, 0.55]
Yombi 2020	91	197	84	164	Adults (≥ 18y)	0.52 [0.44, 0.60]	0.45 [0.40, 0.51]
Sacks 2020	68	897	89	693	Adults (≥ 18y)	0.43 [0.35, 0.51]	0.44 [0.41, 0.46]
Tan 2021	99	109	188	73	Adults (≥ 18y)	0.34 [0.29, 0.40]	0.40 [0.33, 0.48]
Chung 2021	467	2629	449	1416	Adults (≥ 18y)	0.51 [0.48, 0.54]	0.35 [0.34, 0.36]
Vilke 2020	40	438	290	6126	All ages	0.12 [0.09, 0.16]	0.93 [0.93, 0.94]
Raberahona 2020	162	215	1126	1651	All ages	0.13 [0.11, 0.15]	0.88 [0.87, 0.90]
Sonoda 2021	7	111	10	232	All ages	0.41 [0.18, 0.67]	0.68 [0.62, 0.73]
Sun 2020	18	332	36	402	All ages	0.33 [0.21, 0.47]	0.55 [0.51, 0.58]
Zurl 2021	2	227	8	806	Children (< 18y)	0.20 [0.03, 0.56]	0.78 [0.75, 0.81]
Lazzerini 2021	36	881	123	1108	Children (< 18y)	0.23 [0.16, 0.30]	0.56 [0.53, 0.58]



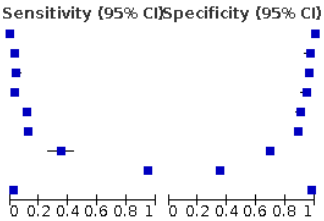
Rhinorrhoea (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	4	1	29	92	Adults (≥ 18y)	0.12 [0.03, 0.28]	0.99 [0.94, 1.00]
Mao 2020	9	59	179	757	Adults (≥ 18y)	0.05 [0.02, 0.09]	0.93 [0.91, 0.94]
Hüfner 2020	3	58	50	599	Adults (≥ 18y)	0.06 [0.01, 0.16]	0.91 [0.89, 0.93]
Nitecki 2021	106	2192	1232	20832	Adults (≥ 18y)	0.08 [0.07, 0.10]	0.90 [0.90, 0.91]
Barbhaya 2021	92	166	754	1459	Adults (≥ 18y)	0.11 [0.09, 0.13]	0.90 [0.88, 0.91]
Huang 2020	14	15	322	124	Adults (≥ 18y)	0.04 [0.02, 0.07]	0.89 [0.83, 0.94]
Arslan 2021	3	28	173	200	Adults (≥ 18y)	0.02 [0.00, 0.05]	0.88 [0.83, 0.92]
Sacks 2020	22	204	135	1386	Adults (≥ 18y)	0.14 [0.09, 0.20]	0.87 [0.85, 0.89]
Chew 2021	6	106	27	599	Adults (≥ 18y)	0.18 [0.07, 0.35]	0.85 [0.82, 0.88]
King 2020	383	105	1604	371	Adults (≥ 18y)	0.19 [0.18, 0.21]	0.78 [0.74, 0.82]
Shah 2020	10	74	23	209	Adults (≥ 18y)	0.30 [0.16, 0.49]	0.74 [0.68, 0.79]
Leung 2021	23	412	63	760	Adults (≥ 18y)	0.27 [0.18, 0.37]	0.65 [0.62, 0.68]
Ide 2021	13	100	12	152	Adults (≥ 18y)	0.52 [0.31, 0.72]	0.60 [0.54, 0.66]
Zayet 2020a	59	77	36	45	Adults (≥ 18y)	0.62 [0.52, 0.72]	0.37 [0.28, 0.46]
Sonoda 2021	5	56	12	287	All ages	0.29 [0.10, 0.56]	0.84 [0.79, 0.87]
Raberahona 2020	400	377	888	1489	All ages	0.31 [0.29, 0.34]	0.80 [0.78, 0.82]
Lazzerini 2021	32	372	127	1617	Children (< 18y)	0.20 [0.14, 0.27]	0.81 [0.80, 0.83]



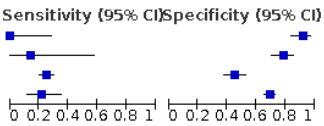
Nasal congestion (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	2	0	626	308	Adults (≥ 18y)	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]
Huang 2020	11	4	325	135	Adults (≥ 18y)	0.03 [0.02, 0.06]	0.97 [0.93, 0.99]
Mao 2020	8	32	180	784	Adults (≥ 18y)	0.04 [0.02, 0.08]	0.96 [0.95, 0.97]
Martín-Sánchez 2020	16	13	424	214	Adults (≥ 18y)	0.04 [0.02, 0.06]	0.94 [0.90, 0.97]
King 2020	241	46	1746	430	Adults (≥ 18y)	0.12 [0.11, 0.14]	0.90 [0.87, 0.93]
Barbhaya 2021	110	189	736	1436	Adults (≥ 18y)	0.13 [0.11, 0.15]	0.88 [0.87, 0.90]
Ahmed 2021	43	516	80	1182	Adults (≥ 18y)	0.35 [0.27, 0.44]	0.70 [0.67, 0.72]
Chung 2021	447	1747	27	940	Adults (≥ 18y)	0.94 [0.92, 0.96]	0.35 [0.33, 0.37]
Raberahona 2020	34	42	1254	1824	All ages	0.03 [0.02, 0.04]	0.98 [0.97, 0.98]



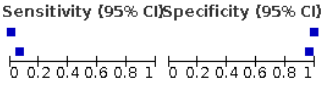
Nasal symptoms (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Peng 2020	0	6	11	69	Adults (≥ 18y)	0.00 [0.00, 0.28]	0.92 [0.83, 0.97]
Feng 2021	1	27	6	98	Adults (≥ 18y)	0.14 [0.00, 0.58]	0.78 [0.70, 0.85]
Tan 2021	72	100	215	82	Adults (≥ 18y)	0.25 [0.20, 0.31]	0.45 [0.38, 0.53]
Sun 2020	12	226	42	508	All ages	0.22 [0.12, 0.36]	0.69 [0.66, 0.73]



Sneezing (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Mao 2020	2	2	186	814	Adults (≥ 18y)	0.01 [0.00, 0.04]	1.00 [0.99, 1.00]
King 2020	132	18	1855	458	Adults (≥ 18y)	0.07 [0.06, 0.08]	0.96 [0.94, 0.98]



Sinusitis (retrospective data collection)

Figure 23. (Continued)

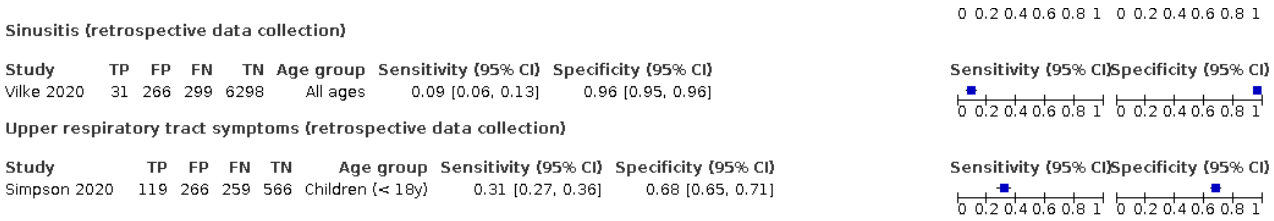
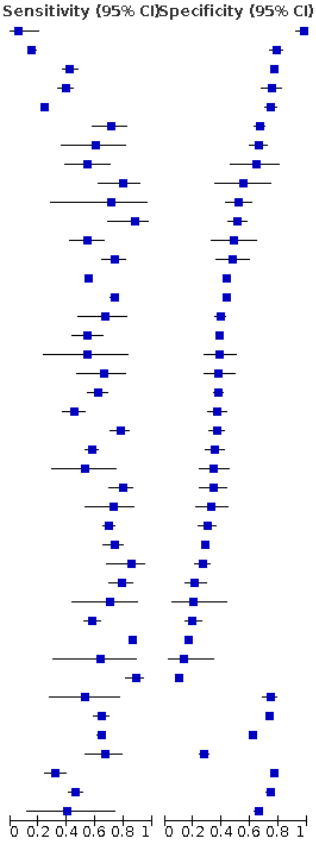


Figure 24. Forest plot of lower respiratory signs/symptoms (retrospective data collection)

Cough (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	2	2	31	91	Adults (≥ 18y)	0.06 [0.01, 0.20]	0.98 [0.92, 1.00]
Wei 2020	98	65	530	243	Adults (≥ 18y)	0.16 [0.13, 0.19]	0.79 [0.74, 0.83]
Aldobyany 2020	143	254	197	841	Adults (≥ 18y)	0.42 [0.37, 0.48]	0.77 [0.74, 0.79]
Huang 2020	132	34	204	105	Adults (≥ 18y)	0.39 [0.34, 0.45]	0.76 [0.68, 0.82]
King 2020	486	121	1501	355	Adults (≥ 18y)	0.24 [0.23, 0.26]	0.75 [0.70, 0.78]
Hüfner 2020	42	199	17	403	Adults (≥ 18y)	0.71 [0.58, 0.82]	0.67 [0.63, 0.71]
Haliga 2021	12	79	8	154	Adults (≥ 18y)	0.60 [0.36, 0.81]	0.66 [0.60, 0.72]
Allegorico 2020	23	12	19	22	Adults (≥ 18y)	0.55 [0.39, 0.70]	0.65 [0.46, 0.80]
Arenas 2020	27	12	7	15	Adults (≥ 18y)	0.79 [0.62, 0.91]	0.56 [0.35, 0.75]
Feng 2021	5	60	2	65	Adults (≥ 18y)	0.71 [0.29, 0.96]	0.52 [0.43, 0.61]
Ide 2021	22	123	3	129	Adults (≥ 18y)	0.88 [0.69, 0.97]	0.51 [0.45, 0.58]
Cunarro-Lopez 2020	37	22	31	21	Adults (≥ 18y)	0.54 [0.42, 0.67]	0.49 [0.33, 0.65]
Langer 2020	91	39	33	36	Adults (≥ 18y)	0.73 [0.65, 0.81]	0.48 [0.36, 0.60]
Nitecki 2021	743	12939	595	10085	Adults (≥ 18y)	0.56 [0.53, 0.58]	0.44 [0.43, 0.44]
Barbhaya 2021	622	916	224	709	Adults (≥ 18y)	0.74 [0.70, 0.76]	0.44 [0.41, 0.46]
Chew 2021	22	427	11	278	Adults (≥ 18y)	0.67 [0.48, 0.82]	0.39 [0.36, 0.43]
Leung 2021	47	718	39	454	Adults (≥ 18y)	0.55 [0.44, 0.65]	0.39 [0.36, 0.42]
Peng 2020	6	46	5	29	Adults (≥ 18y)	0.55 [0.23, 0.83]	0.39 [0.28, 0.51]
Zhu 2020	21	52	11	32	Adults (≥ 18y)	0.66 [0.47, 0.81]	0.38 [0.28, 0.49]
Mao 2020	116	506	72	310	Adults (≥ 18y)	0.62 [0.54, 0.69]	0.38 [0.35, 0.41]
Arslan 2021	79	144	97	84	Adults (≥ 18y)	0.45 [0.37, 0.53]	0.37 [0.31, 0.43]
Yombi 2020	136	229	39	132	Adults (≥ 18y)	0.78 [0.71, 0.84]	0.37 [0.32, 0.42]
Chan 2021	293	137	217	74	Adults (≥ 18y)	0.57 [0.53, 0.62]	0.35 [0.29, 0.42]
Xie 2020	11	55	10	29	Adults (≥ 18y)	0.52 [0.30, 0.74]	0.35 [0.24, 0.46]
Tordjman 2020	79	66	21	34	Adults (≥ 18y)	0.79 [0.70, 0.87]	0.34 [0.25, 0.44]
Vieceli 2020	21	48	8	23	Adults (≥ 18y)	0.72 [0.53, 0.87]	0.32 [0.22, 0.45]
Martín-Sánchez 2020	306	159	134	68	Adults (≥ 18y)	0.70 [0.65, 0.74]	0.30 [0.24, 0.36]
Sacks 2020	115	1136	42	454	Adults (≥ 18y)	0.73 [0.66, 0.80]	0.29 [0.26, 0.31]
Shah 2020	28	208	5	75	Adults (≥ 18y)	0.85 [0.68, 0.95]	0.27 [0.21, 0.32]
Zayet 2020a	75	96	20	26	Adults (≥ 18y)	0.79 [0.69, 0.87]	0.21 [0.14, 0.30]
Pisapia 2020	12	16	5	4	Adults (≥ 18y)	0.71 [0.44, 0.90]	0.20 [0.06, 0.44]
Tan 2021	166	146	121	36	Adults (≥ 18y)	0.58 [0.52, 0.64]	0.20 [0.14, 0.26]
Chung 2021	788	3357	128	688	Adults (≥ 18y)	0.86 [0.84, 0.88]	0.17 [0.16, 0.18]
Cheng 2020	7	19	4	3	Adults (≥ 18y)	0.64 [0.31, 0.89]	0.14 [0.03, 0.35]
Ahmed 2021	109	1520	14	178	Adults (≥ 18y)	0.89 [0.82, 0.94]	0.10 [0.09, 0.12]
Sonoda 2021	9	89	8	254	All ages	0.53 [0.28, 0.77]	0.74 [0.69, 0.79]
Vilke 2020	213	1748	117	4816	All ages	0.65 [0.59, 0.70]	0.73 [0.72, 0.74]
Raberahona 2020	826	719	462	1147	All ages	0.64 [0.61, 0.67]	0.61 [0.59, 0.64]
Sun 2020	36	528	18	206	All ages	0.67 [0.53, 0.79]	0.28 [0.25, 0.31]
Lazzerini 2021	51	452	108	1537	Children (< 18y)	0.32 [0.25, 0.40]	0.77 [0.75, 0.79]
Simpson 2020	175	213	203	619	Children (< 18y)	0.46 [0.41, 0.51]	0.74 [0.71, 0.77]
Zurl 2021	4	357	6	685	Children (< 18y)	0.40 [0.12, 0.74]	0.66 [0.63, 0.69]



Dyspnoea (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	6	2	622	306	Adults (≥ 18y)	0.01 [0.00, 0.02]	0.99 [0.98, 1.00]
King 2020	31	6	1956	470	Adults (≥ 18y)	0.02 [0.01, 0.02]	0.99 [0.97, 1.00]
Zhu 2020	3	2	29	82	Adults (≥ 18y)	0.09 [0.02, 0.25]	0.98 [0.92, 1.00]
Fiel-Ozores 2021	4	3	29	90	Adults (≥ 18y)	0.12 [0.03, 0.28]	0.97 [0.91, 0.99]
Mao 2020	12	51	176	765	Adults (≥ 18y)	0.06 [0.03, 0.11]	0.94 [0.92, 0.95]
Aldobyany 2020	51	84	289	1011	Adults (≥ 18y)	0.15 [0.11, 0.19]	0.92 [0.91, 0.94]
Huang 2020	33	12	303	127	Adults (≥ 18y)	0.10 [0.07, 0.14]	0.91 [0.85, 0.95]
Peng 2020	0	10	11	65	Adults (≥ 18y)	0.00 [0.00, 0.28]	0.87 [0.77, 0.93]
Feng 2021	0	18	7	107	Adults (≥ 18y)	0.00 [0.00, 0.41]	0.86 [0.78, 0.91]
Cheng 2020	1	4	10	18	Adults (≥ 18y)	0.09 [0.00, 0.41]	0.82 [0.60, 0.95]
Arslan 2021	6	43	170	185	Adults (≥ 18y)	0.03 [0.01, 0.07]	0.81 [0.75, 0.86]
Ide 2021	2	49	23	203	Adults (≥ 18y)	0.08 [0.01, 0.26]	0.81 [0.75, 0.85]
Pisapia 2020	7	4	10	16	Adults (≥ 18y)	0.41 [0.18, 0.67]	0.80 [0.56, 0.94]
Sacks 2020	39	444	118	1146	Adults (≥ 18y)	0.25 [0.18, 0.32]	0.72 [0.70, 0.74]
Chew 2021	4	207	29	498	Adults (≥ 18y)	0.12 [0.03, 0.28]	0.71 [0.67, 0.74]
Cunarro-Lopez 2020	20	13	48	30	Adults (≥ 18y)	0.29 [0.19, 0.42]	0.70 [0.54, 0.83]
Arenas 2020	23	9	11	18	Adults (≥ 18y)	0.68 [0.49, 0.83]	0.67 [0.46, 0.83]
Chan 2021	108	71	402	140	Adults (≥ 18y)	0.21 [0.18, 0.25]	0.66 [0.60, 0.73]
Yombi 2020	65	122	110	239	Adults (≥ 18y)	0.37 [0.30, 0.45]	0.66 [0.61, 0.71]
Martín-Sánchez 2020	140	82	300	145	Adults (≥ 18y)	0.32 [0.27, 0.36]	0.64 [0.57, 0.70]
Barbhaya 2021	297	589	549	1036	Adults (≥ 18y)	0.35 [0.32, 0.38]	0.64 [0.61, 0.66]
Hüfner 2020	35	236	29	397	Adults (≥ 18y)	0.55 [0.42, 0.67]	0.63 [0.59, 0.66]
Zayet 2020a	40	50	55	72	Adults (≥ 18y)	0.42 [0.32, 0.53]	0.59 [0.50, 0.68]
Langer 2020	43	32	81	43	Adults (≥ 18y)	0.35 [0.26, 0.44]	0.57 [0.45, 0.69]
Chung 2021	366	1901	550	2144	Adults (≥ 18y)	0.40 [0.37, 0.43]	0.53 [0.51, 0.55]
Haliga 2021	7	132	13	101	Adults (≥ 18y)	0.35 [0.15, 0.59]	0.43 [0.37, 0.50]
Shah 2020	23	171	10	112	Adults (≥ 18y)	0.70 [0.51, 0.84]	0.40 [0.34, 0.46]
Vieceli 2020	20	45	9	26	Adults (≥ 18y)	0.69 [0.49, 0.85]	0.37 [0.25, 0.49]
Ahmed 2021	63	1110	60	588	Adults (≥ 18y)	0.51 [0.42, 0.60]	0.35 [0.32, 0.37]
Tordjman 2020	70	69	30	31	Adults (≥ 18y)	0.70 [0.60, 0.79]	0.31 [0.22, 0.41]
Allegorico 2020	31	26	11	8	Adults (≥ 18y)	0.74 [0.58, 0.86]	0.24 [0.11, 0.41]
Sonoda 2021	2	40	15	303	All ages	0.12 [0.01, 0.36]	0.88 [0.84, 0.92]
Sun 2020	7	93	47	641	All ages	0.13 [0.05, 0.25]	0.87 [0.85, 0.90]
Raberahona 2020	199	257	1089	1609	All ages	0.15 [0.14, 0.18]	0.86 [0.85, 0.88]
Vilke 2020	154	1890	176	4674	All ages	0.47 [0.41, 0.52]	0.71 [0.70, 0.72]
Zurl 2021	0	113	10	927	Children (< 18y)	0.00 [0.00, 0.31]	0.89 [0.87, 0.91]
Lazzerini 2021	12	255	147	1734	Children (< 18y)	0.08 [0.04, 0.13]	0.87 [0.86, 0.89]

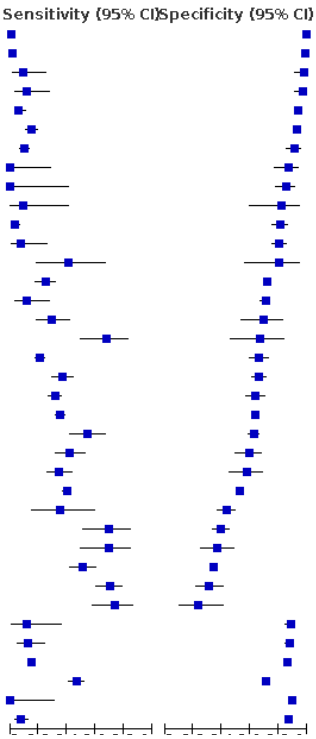
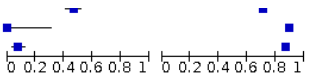


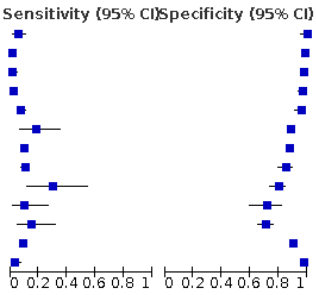
Figure 24. (Continued)

Vilke 2020	154	1890	176	4674	All ages	0.47 [0.41, 0.52]	0.71 [0.70, 0.72]
Zurl 2021	0	113	10	927	Children (< 18y)	0.00 [0.00, 0.31]	0.89 [0.87, 0.91]
Lazzerini 2021	12	255	147	1734	Children (< 18y)	0.08 [0.04, 0.13]	0.87 [0.86, 0.89]



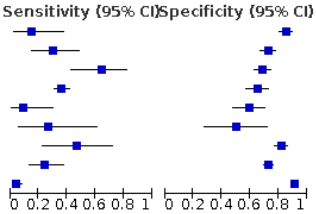
Chest tightness/pain (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Langer 2020	7	0	117	75	Adults (≥ 18y)	0.06 [0.02, 0.11]	1.00 [0.95, 1.00]
Nitecki 2021	24	406	1314	22618	Adults (≥ 18y)	0.02 [0.01, 0.03]	0.98 [0.98, 0.98]
Mao 2020	4	19	184	797	Adults (≥ 18y)	0.02 [0.01, 0.05]	0.98 [0.96, 0.99]
Wei 2020	15	10	613	298	Adults (≥ 18y)	0.02 [0.01, 0.04]	0.97 [0.94, 0.98]
Huang 2020	27	6	309	133	Adults (≥ 18y)	0.08 [0.05, 0.11]	0.96 [0.91, 0.98]
Chew 2021	6	81	27	624	Adults (≥ 18y)	0.18 [0.07, 0.35]	0.89 [0.86, 0.91]
Barbhaya 2021	89	193	757	1432	Adults (≥ 18y)	0.11 [0.09, 0.13]	0.88 [0.86, 0.90]
Martín-Sánchez 2020	47	34	393	193	Adults (≥ 18y)	0.11 [0.08, 0.14]	0.85 [0.80, 0.89]
Haliga 2021	6	47	14	186	Adults (≥ 18y)	0.30 [0.12, 0.54]	0.80 [0.74, 0.85]
Vieceli 2020	3	20	26	51	Adults (≥ 18y)	0.10 [0.02, 0.27]	0.72 [0.60, 0.82]
Shah 2020	5	81	28	202	Adults (≥ 18y)	0.15 [0.05, 0.32]	0.71 [0.66, 0.77]
Raberahona 2020	118	178	1170	1688	All ages	0.09 [0.08, 0.11]	0.90 [0.89, 0.92]
Lazzerini 2021	6	44	153	1945	Children (< 18y)	0.04 [0.01, 0.08]	0.98 [0.97, 0.98]



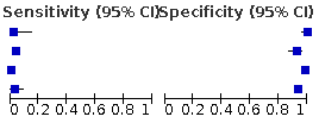
Sputum production/productive cough (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	3	34	17	199	Adults (≥ 18y)	0.15 [0.03, 0.38]	0.85 [0.80, 0.90]
Shah 2020	10	77	23	206	Adults (≥ 18y)	0.30 [0.16, 0.49]	0.73 [0.67, 0.78]
Ide 2021	16	79	9	173	Adults (≥ 18y)	0.64 [0.43, 0.82]	0.69 [0.63, 0.74]
Huang 2020	122	48	214	91	Adults (≥ 18y)	0.36 [0.31, 0.42]	0.65 [0.57, 0.73]
Xie 2020	2	34	19	50	Adults (≥ 18y)	0.10 [0.01, 0.30]	0.60 [0.48, 0.70]
Cheng 2020	3	11	8	11	Adults (≥ 18y)	0.27 [0.06, 0.61]	0.50 [0.28, 0.72]
Sonoda 2021	8	62	9	281	All ages	0.47 [0.23, 0.72]	0.82 [0.77, 0.86]
Sun 2020	13	199	41	535	All ages	0.24 [0.13, 0.38]	0.73 [0.70, 0.76]
Lazzerini 2021	7	185	152	1804	Children (< 18y)	0.04 [0.02, 0.09]	0.91 [0.89, 0.92]



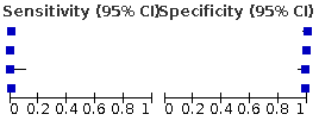
Wheeze (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	1	0	32	93	Adults (≥ 18y)	0.03 [0.00, 0.16]	1.00 [0.96, 1.00]
Huang 2020	15	10	321	129	Adults (≥ 18y)	0.04 [0.03, 0.07]	0.93 [0.87, 0.96]
Raberahona 2020	10	29	1278	1837	All ages	0.01 [0.00, 0.01]	0.98 [0.98, 0.99]
Lazzerini 2021	3	120	83	1706	Children (< 18y)	0.03 [0.01, 0.10]	0.93 [0.92, 0.95]



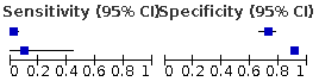
Haemoptysis (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	3	0	333	139	Adults (≥ 18y)	0.01 [0.00, 0.03]	1.00 [0.97, 1.00]
Mao 2020	1	7	187	809	Adults (≥ 18y)	0.01 [0.00, 0.03]	0.99 [0.98, 1.00]
Zhu 2020	0	1	32	83	Adults (≥ 18y)	0.00 [0.00, 0.11]	0.99 [0.94, 1.00]
Raberahona 2020	16	26	1272	1840	All ages	0.01 [0.01, 0.02]	0.99 [0.98, 0.99]



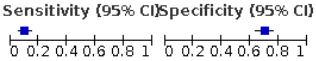
Pulmonary auscultation: rhonchi (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	5	63	171	165	Adults (≥ 18y)	0.03 [0.01, 0.07]	0.72 [0.66, 0.78]
Zurl 2021	1	88	9	942	Children (< 18y)	0.10 [0.00, 0.45]	0.91 [0.90, 0.93]



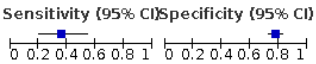
Pulmonary auscultation: crackling (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	18	68	158	160	Adults (≥ 18y)	0.10 [0.06, 0.16]	0.70 [0.64, 0.76]



Dry cough (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Shah 2020	12	62	21	221	Adults (≥ 18y)	0.36 [0.20, 0.55]	0.78 [0.73, 0.83]



Respiratory distress (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Vieceli 2020	2	16	27	55	Adults (≥ 18y)	0.07 [0.01, 0.23]	0.77 [0.66, 0.87]

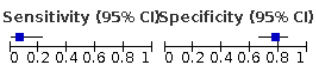
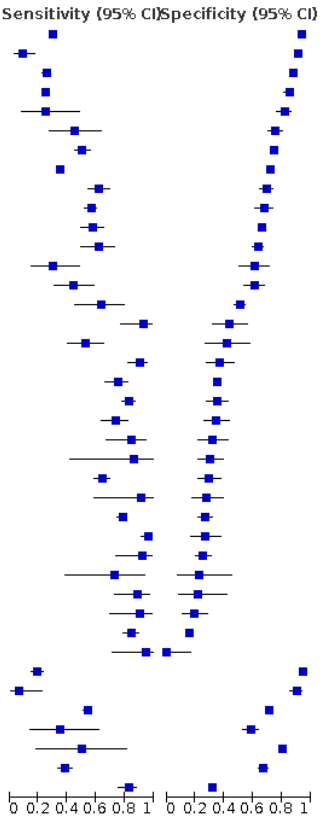


Figure 25. Forest plot of systemic signs/symptoms (retrospective data collection)

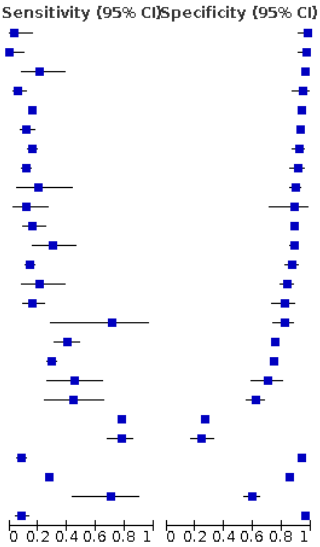
Fever (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Clifford 2020	1947	702	4577	9641	Adults (≥ 18y)	0.30 [0.29, 0.31]	0.93 [0.93, 0.94]
Leung 2021	8	102	78	1070	Adults (≥ 18y)	0.09 [0.04, 0.18]	0.91 [0.90, 0.93]
Barbhaya 2021	219	206	627	1419	Adults (≥ 18y)	0.26 [0.23, 0.29]	0.87 [0.86, 0.89]
King 2020	506	72	1481	404	Adults (≥ 18y)	0.25 [0.24, 0.27]	0.85 [0.81, 0.88]
Haliga 2021	5	43	15	190	Adults (≥ 18y)	0.25 [0.09, 0.49]	0.82 [0.76, 0.86]
Shah 2020	15	69	18	214	Adults (≥ 18y)	0.45 [0.28, 0.64]	0.76 [0.70, 0.81]
Aldobyany 2020	172	278	168	817	Adults (≥ 18y)	0.51 [0.45, 0.56]	0.75 [0.72, 0.77]
Nitecki 2021	470	6424	868	16600	Adults (≥ 18y)	0.35 [0.33, 0.38]	0.72 [0.72, 0.73]
Yombi 2020	109	111	66	250	Adults (≥ 18y)	0.62 [0.55, 0.69]	0.69 [0.64, 0.74]
Chan 2021	288	68	222	143	Adults (≥ 18y)	0.56 [0.52, 0.61]	0.68 [0.61, 0.74]
Sacks 2020	90	534	67	1056	Adults (≥ 18y)	0.57 [0.49, 0.65]	0.66 [0.64, 0.69]
Hüfner 2020	47	230	29	397	Adults (≥ 18y)	0.62 [0.50, 0.73]	0.63 [0.59, 0.67]
Fiel-Ozores 2021	10	36	23	57	Adults (≥ 18y)	0.30 [0.16, 0.49]	0.61 [0.51, 0.71]
Kim 2020	24	73	30	115	Adults (≥ 18y)	0.44 [0.31, 0.59]	0.61 [0.54, 0.68]
Chew 2021	21	347	12	358	Adults (≥ 18y)	0.64 [0.45, 0.80]	0.51 [0.47, 0.55]
Vieceli 2020	27	40	2	31	Adults (≥ 18y)	0.93 [0.77, 0.99]	0.44 [0.32, 0.56]
Cunarro-Lopez 2020	36	25	32	18	Adults (≥ 18y)	0.53 [0.40, 0.65]	0.42 [0.27, 0.58]
Tordjman 2020	90	63	10	37	Adults (≥ 18y)	0.90 [0.82, 0.95]	0.37 [0.28, 0.47]
Ahmed 2021	92	1095	31	603	Adults (≥ 18y)	0.75 [0.66, 0.82]	0.36 [0.33, 0.38]
Tan 2021	237	118	50	64	Adults (≥ 18y)	0.83 [0.78, 0.87]	0.35 [0.28, 0.43]
Zayet 2020a	70	80	25	42	Adults (≥ 18y)	0.74 [0.64, 0.82]	0.34 [0.26, 0.44]
Zhu 2020	27	57	5	27	Adults (≥ 18y)	0.84 [0.67, 0.95]	0.32 [0.22, 0.43]
Feng 2021	6	87	1	38	Adults (≥ 18y)	0.86 [0.42, 1.00]	0.30 [0.22, 0.39]
Huang 2020	216	98	120	41	Adults (≥ 18y)	0.64 [0.59, 0.69]	0.29 [0.22, 0.38]
Peng 2020	10	54	1	21	Adults (≥ 18y)	0.91 [0.59, 1.00]	0.28 [0.18, 0.40]
Wei 2020	491	225	137	83	Adults (≥ 18y)	0.78 [0.75, 0.81]	0.27 [0.22, 0.32]
Langer 2020	119	55	5	20	Adults (≥ 18y)	0.96 [0.91, 0.99]	0.27 [0.17, 0.38]
Ide 2021	23	188	2	64	Adults (≥ 18y)	0.92 [0.74, 0.99]	0.25 [0.20, 0.31]
Cheng 2020	8	17	3	5	Adults (≥ 18y)	0.73 [0.39, 0.94]	0.23 [0.08, 0.45]
Arenas 2020	30	21	4	6	Adults (≥ 18y)	0.88 [0.73, 0.97]	0.22 [0.09, 0.42]
Xie 2020	19	68	2	16	Adults (≥ 18y)	0.90 [0.70, 0.99]	0.19 [0.11, 0.29]
Mao 2020	159	684	29	132	Adults (≥ 18y)	0.85 [0.79, 0.89]	0.16 [0.14, 0.19]
Pisapia 2020	16	20	1	0	Adults (≥ 18y)	0.94 [0.71, 1.00]	0.00 [0.00, 0.17]
Vilke 2020	64	368	266	6196	All ages	0.19 [0.15, 0.24]	0.94 [0.94, 0.95]
Tolia 2020	2	25	27	227	All ages	0.07 [0.01, 0.23]	0.90 [0.86, 0.93]
Raberahona 2020	695	543	593	1323	All ages	0.54 [0.51, 0.57]	0.71 [0.69, 0.73]
Sonoda 2021	6	142	11	201	All ages	0.35 [0.14, 0.62]	0.59 [0.53, 0.64]
Zurl 2021	5	205	5	851	Children (< 18y)	0.50 [0.19, 0.81]	0.81 [0.78, 0.83]
Simpson 2020	147	276	231	556	Children (< 18y)	0.39 [0.34, 0.44]	0.67 [0.64, 0.70]
Lazzerini 2021	131	1355	28	634	Children (< 18y)	0.82 [0.76, 0.88]	0.32 [0.30, 0.34]



Headache (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Zhu 2020	1	2	31	82	Adults (≥ 18y)	0.03 [0.00, 0.16]	0.98 [0.92, 1.00]
Fiel-Ozores 2021	0	3	33	90	Adults (≥ 18y)	0.00 [0.00, 0.11]	0.97 [0.91, 0.99]
Chew 2021	7	25	26	680	Adults (≥ 18y)	0.21 [0.09, 0.39]	0.96 [0.95, 0.98]
Langer 2020	8	4	116	71	Adults (≥ 18y)	0.06 [0.03, 0.12]	0.95 [0.87, 0.99]
King 2020	312	30	1675	446	Adults (≥ 18y)	0.16 [0.14, 0.17]	0.94 [0.91, 0.96]
Mao 2020	23	61	165	755	Adults (≥ 18y)	0.12 [0.08, 0.18]	0.93 [0.91, 0.94]
Chan 2021	82	17	428	194	Adults (≥ 18y)	0.16 [0.13, 0.20]	0.92 [0.87, 0.95]
Huang 2020	39	12	297	127	Adults (≥ 18y)	0.12 [0.08, 0.16]	0.91 [0.85, 0.95]
Haliga 2021	4	24	16	209	Adults (≥ 18y)	0.20 [0.06, 0.44]	0.90 [0.85, 0.93]
Arenas 2020	4	3	30	24	Adults (≥ 18y)	0.12 [0.03, 0.27]	0.89 [0.71, 0.98]
Leung 2021	14	131	72	1041	Adults (≥ 18y)	0.16 [0.09, 0.26]	0.89 [0.87, 0.91]
Hüfner 2020	12	69	28	527	Adults (≥ 18y)	0.30 [0.17, 0.47]	0.88 [0.86, 0.91]
Martín-Sánchez 2020	63	30	377	197	Adults (≥ 18y)	0.14 [0.11, 0.18]	0.87 [0.82, 0.91]
Shah 2020	7	47	26	236	Adults (≥ 18y)	0.21 [0.09, 0.39]	0.83 [0.79, 0.88]
Tordjman 2020	16	18	84	82	Adults (≥ 18y)	0.16 [0.09, 0.25]	0.82 [0.73, 0.89]
Feng 2021	5	23	2	102	Adults (≥ 18y)	0.71 [0.29, 0.96]	0.82 [0.74, 0.88]
Ahmed 2021	49	428	74	1270	Adults (≥ 18y)	0.40 [0.31, 0.49]	0.75 [0.73, 0.77]
Barbhaya 2021	249	416	597	1209	Adults (≥ 18y)	0.29 [0.26, 0.33]	0.74 [0.72, 0.77]
Vieceli 2020	13	21	16	50	Adults (≥ 18y)	0.45 [0.26, 0.64]	0.70 [0.58, 0.81]
Ide 2021	11	96	14	156	Adults (≥ 18y)	0.44 [0.24, 0.65]	0.62 [0.56, 0.68]
Chung 2021	714	2953	202	1092	Adults (≥ 18y)	0.78 [0.75, 0.81]	0.27 [0.26, 0.28]
Zayet 2020a	74	92	21	30	Adults (≥ 18y)	0.78 [0.68, 0.86]	0.25 [0.17, 0.33]
Vilke 2020	27	434	303	6130	All ages	0.08 [0.05, 0.12]	0.93 [0.93, 0.94]
Raberahona 2020	358	276	930	1590	All ages	0.28 [0.25, 0.30]	0.85 [0.84, 0.87]
Sonoda 2021	12	140	5	203	All ages	0.71 [0.44, 0.90]	0.59 [0.54, 0.64]
Lazzerini 2021	13	79	146	1910	Children (< 18y)	0.08 [0.04, 0.14]	0.96 [0.95, 0.97]



Myalgia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	8	2	620	306	Adults (≥ 18y)	0.01 [0.01, 0.02]	0.99 [0.98, 1.00]
Fiel-Ozores 2021	0	2	33	91	Adults (≥ 18y)	0.00 [0.00, 0.11]	0.98 [0.92, 1.00]
Leung 2021	8	69	78	1103	Adults (≥ 18y)	0.09 [0.04, 0.18]	0.94 [0.93, 0.95]
Xie 2020	1	6	20	78	Adults (≥ 18y)	0.05 [0.00, 0.24]	0.93 [0.85, 0.97]
Haliga 2021	7	19	13	214	Adults (≥ 18y)	0.35 [0.15, 0.59]	0.92 [0.88, 0.95]
Huang 2020	39	14	297	125	Adults (≥ 18y)	0.12 [0.08, 0.16]	0.90 [0.84, 0.94]
Tan 2021	69	19	218	163	Adults (≥ 18y)	0.24 [0.19, 0.29]	0.90 [0.84, 0.94]
Arenas 2020	13	3	21	24	Adults (≥ 18y)	0.38 [0.22, 0.56]	0.89 [0.71, 0.98]

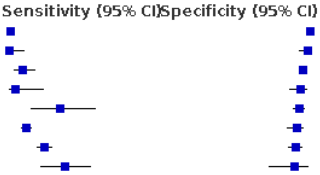
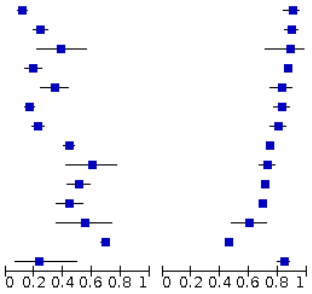


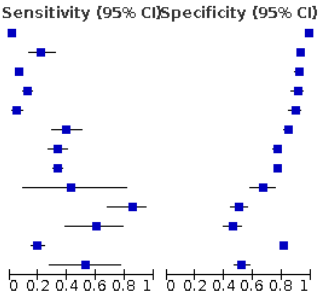
Figure 25. (Continued)

Huang 2020	39	14	297	125	Adults (≥ 18y)	0.12 [0.08, 0.16]	0.90 [0.84, 0.94]
Tan 2021	69	19	218	163	Adults (≥ 18y)	0.24 [0.19, 0.29]	0.90 [0.84, 0.94]
Arenas 2020	13	3	21	24	Adults (≥ 18y)	0.38 [0.22, 0.56]	0.89 [0.71, 0.98]
Mao 2020	36	105	152	711	Adults (≥ 18y)	0.19 [0.14, 0.26]	0.87 [0.85, 0.89]
Tordjman 2020	34	17	66	83	Adults (≥ 18y)	0.34 [0.25, 0.44]	0.83 [0.74, 0.90]
Chan 2021	87	36	423	175	Adults (≥ 18y)	0.17 [0.14, 0.21]	0.83 [0.77, 0.88]
Martín-Sánchez 2020	99	44	341	183	Adults (≥ 18y)	0.23 [0.19, 0.27]	0.81 [0.75, 0.86]
Barbhaya 2021	374	417	472	1208	Adults (≥ 18y)	0.44 [0.41, 0.48]	0.74 [0.72, 0.76]
Shah 2020	20	77	13	206	Adults (≥ 18y)	0.61 [0.42, 0.77]	0.73 [0.67, 0.78]
Sacks 2020	80	459	77	1131	Adults (≥ 18y)	0.51 [0.43, 0.59]	0.71 [0.69, 0.73]
Ahmed 2021	55	526	68	1172	Adults (≥ 18y)	0.45 [0.36, 0.54]	0.69 [0.67, 0.71]
Vieceli 2020	16	28	13	43	Adults (≥ 18y)	0.55 [0.36, 0.74]	0.61 [0.48, 0.72]
Chung 2021	632	2184	284	1861	Adults (≥ 18y)	0.69 [0.66, 0.72]	0.46 [0.44, 0.48]
Sonoda 2021	4	54	13	289	All ages	0.24 [0.07, 0.50]	0.84 [0.80, 0.88]



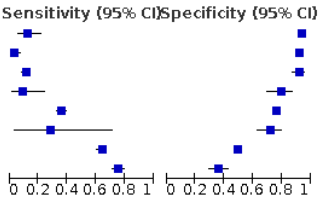
Fatigue (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
King 2020	31	6	1956	470	Adults (≥ 18y)	0.02 [0.01, 0.02]	0.99 [0.97, 1.00]
Leung 2021	19	87	67	1085	Adults (≥ 18y)	0.22 [0.14, 0.32]	0.93 [0.91, 0.94]
Wei 2020	42	24	586	284	Adults (≥ 18y)	0.07 [0.05, 0.09]	0.92 [0.89, 0.95]
Chan 2021	65	19	445	192	Adults (≥ 18y)	0.13 [0.10, 0.16]	0.91 [0.86, 0.94]
Arslan 2021	9	24	167	204	Adults (≥ 18y)	0.05 [0.02, 0.09]	0.89 [0.85, 0.93]
Hüfner 2020	36	106	55	573	Adults (≥ 18y)	0.40 [0.29, 0.50]	0.84 [0.81, 0.87]
Mao 2020	63	187	125	629	Adults (≥ 18y)	0.34 [0.27, 0.41]	0.77 [0.74, 0.80]
Barbhaya 2021	286	377	560	1248	Adults (≥ 18y)	0.34 [0.31, 0.37]	0.77 [0.75, 0.79]
Feng 2021	3	41	4	84	Adults (≥ 18y)	0.43 [0.10, 0.82]	0.67 [0.58, 0.75]
Shah 2020	28	140	5	143	Adults (≥ 18y)	0.85 [0.68, 0.95]	0.51 [0.45, 0.56]
Ide 2021	15	137	10	115	Adults (≥ 18y)	0.60 [0.39, 0.79]	0.46 [0.39, 0.52]
Vilke 2020	65	1254	265	5310	All ages	0.20 [0.16, 0.24]	0.81 [0.80, 0.82]
Sonoda 2021	9	164	8	179	All ages	0.53 [0.28, 0.77]	0.52 [0.47, 0.58]



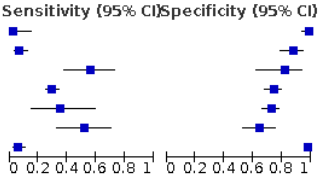
Chills/shivers (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Leung 2021	11	75	75	1097	Adults (≥ 18y)	0.13 [0.07, 0.22]	0.94 [0.92, 0.95]
Mao 2020	7	64	181	752	Adults (≥ 18y)	0.04 [0.02, 0.08]	0.92 [0.90, 0.94]
Chan 2021	59	17	451	194	Adults (≥ 18y)	0.12 [0.09, 0.15]	0.92 [0.87, 0.95]
Fiel-Ozores 2021	3	19	30	74	Adults (≥ 18y)	0.09 [0.02, 0.24]	0.80 [0.70, 0.87]
Barbhaya 2021	306	395	540	1230	Adults (≥ 18y)	0.36 [0.33, 0.40]	0.76 [0.74, 0.78]
Feng 2021	2	35	5	90	Adults (≥ 18y)	0.29 [0.04, 0.71]	0.72 [0.63, 0.80]
Chung 2021	586	2063	330	1982	Adults (≥ 18y)	0.64 [0.61, 0.67]	0.49 [0.47, 0.51]
Martín-Sánchez 2020	332	145	108	82	Adults (≥ 18y)	0.75 [0.71, 0.79]	0.36 [0.30, 0.43]



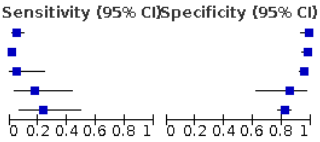
Asthenia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	1	1	32	92	Adults (≥ 18y)	0.03 [0.00, 0.16]	0.99 [0.94, 1.00]
Langer 2020	9	9	115	66	Adults (≥ 18y)	0.07 [0.03, 0.13]	0.88 [0.78, 0.94]
Arenas 2020	19	5	15	22	Adults (≥ 18y)	0.56 [0.38, 0.73]	0.81 [0.62, 0.94]
Martín-Sánchez 2020	131	59	309	168	Adults (≥ 18y)	0.30 [0.26, 0.34]	0.74 [0.68, 0.80]
Haliga 2021	7	64	13	169	Adults (≥ 18y)	0.35 [0.15, 0.59]	0.73 [0.66, 0.78]
Vieceli 2020	15	25	14	46	Adults (≥ 18y)	0.52 [0.33, 0.71]	0.65 [0.53, 0.76]
Lazzerini 2021	10	38	149	1951	Children (< 18y)	0.06 [0.03, 0.11]	0.98 [0.97, 0.99]



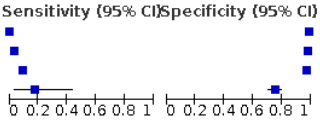
Arthralgia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Langer 2020	6	1	118	74	Adults (≥ 18y)	0.05 [0.02, 0.10]	0.99 [0.93, 1.00]
Huang 2020	6	3	330	136	Adults (≥ 18y)	0.02 [0.01, 0.04]	0.98 [0.94, 1.00]
Haliga 2021	1	11	19	222	Adults (≥ 18y)	0.05 [0.00, 0.25]	0.95 [0.92, 0.98]
Pisapia 2020	3	3	14	17	Adults (≥ 18y)	0.18 [0.04, 0.43]	0.85 [0.62, 0.97]
Sonoda 2021	4	62	13	281	All ages	0.24 [0.07, 0.50]	0.82 [0.77, 0.86]



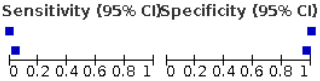
Anorexia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	3	4	625	304	Adults (≥ 18y)	0.00 [0.00, 0.01]	0.99 [0.97, 1.00]
King 2020	75	10	1912	466	Adults (≥ 18y)	0.04 [0.03, 0.05]	0.98 [0.96, 0.99]
Barbhaya 2021	76	50	770	1575	Adults (≥ 18y)	0.09 [0.07, 0.11]	0.97 [0.96, 0.98]
Sonoda 2021	3	85	14	258	All ages	0.18 [0.04, 0.43]	0.75 [0.70, 0.80]



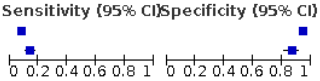
Dizziness (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	1	0	627	308	Adults (≥ 18y)	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]
Barbhaya 2021	36	50	810	1575	Adults (≥ 18y)	0.04 [0.03, 0.06]	0.97 [0.96, 0.98]



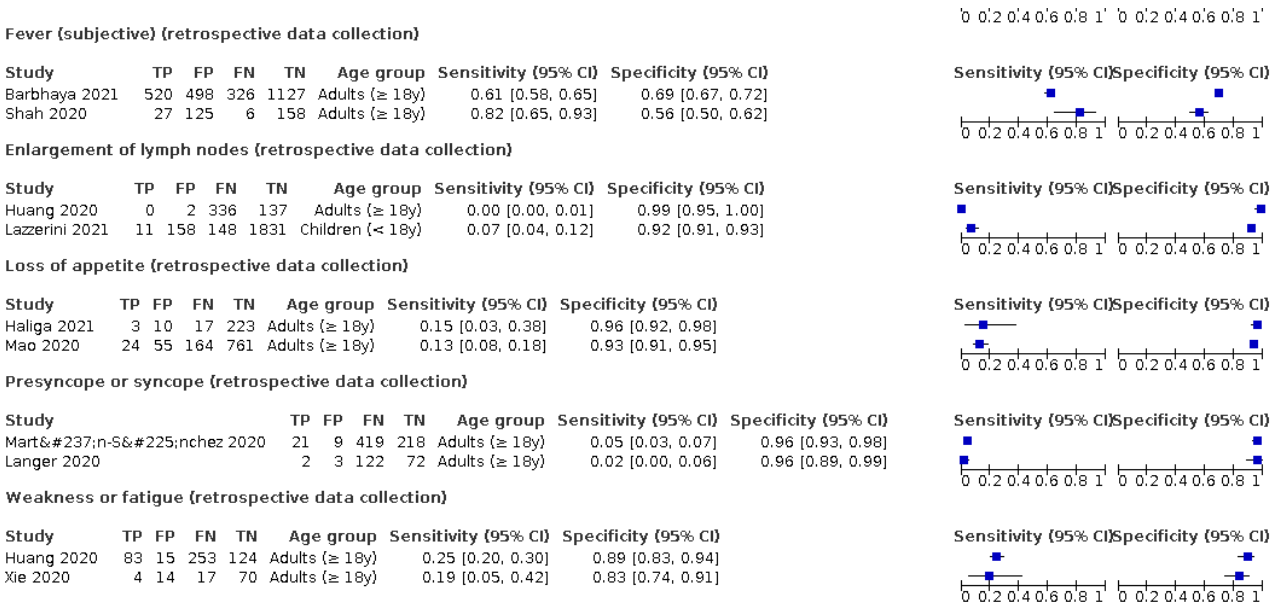
Malaise (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
King 2020	165	25	1822	451	Adults (≥ 18y)	0.08 [0.07, 0.10]	0.95 [0.92, 0.97]
Chan 2021	74	28	436	183	Adults (≥ 18y)	0.15 [0.12, 0.18]	0.87 [0.81, 0.91]



Fever (subjective) (retrospective data collection)

Figure 25. (Continued)



Fever (subjective) (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	520	498	326	1127	Adults (≥ 18y)	0.61 [0.58, 0.65]	0.69 [0.67, 0.72]
Shah 2020	27	125	6	158	Adults (≥ 18y)	0.82 [0.65, 0.93]	0.56 [0.50, 0.62]

Enlargement of lymph nodes (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	0	2	336	137	Adults (≥ 18y)	0.00 [0.00, 0.01]	0.99 [0.95, 1.00]
Lazzerini 2021	11	158	148	1831	Children (< 18y)	0.07 [0.04, 0.12]	0.92 [0.91, 0.93]

Loss of appetite (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	3	10	17	223	Adults (≥ 18y)	0.15 [0.03, 0.38]	0.96 [0.92, 0.98]
Mao 2020	24	55	164	761	Adults (≥ 18y)	0.13 [0.08, 0.18]	0.93 [0.91, 0.95]

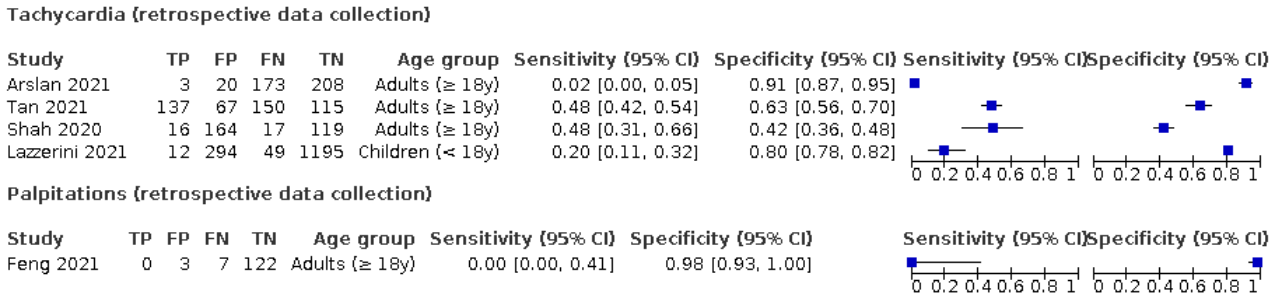
Presyncope or syncope (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Martín-Sánchez 2020	21	9	419	218	Adults (≥ 18y)	0.05 [0.03, 0.07]	0.96 [0.93, 0.98]
Langer 2020	2	3	122	72	Adults (≥ 18y)	0.02 [0.00, 0.06]	0.96 [0.89, 0.99]

Weakness or fatigue (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	83	15	253	124	Adults (≥ 18y)	0.25 [0.20, 0.30]	0.89 [0.83, 0.94]
Xie 2020	4	14	17	70	Adults (≥ 18y)	0.19 [0.05, 0.42]	0.83 [0.74, 0.91]

Figure 26. Forest plot of cardiovascular signs/symptoms (retrospective data collection)



Tachycardia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	3	20	173	208	Adults (≥ 18y)	0.02 [0.00, 0.05]	0.91 [0.87, 0.95]
Tan 2021	137	67	150	115	Adults (≥ 18y)	0.48 [0.42, 0.54]	0.63 [0.56, 0.70]
Shah 2020	16	164	17	119	Adults (≥ 18y)	0.48 [0.31, 0.66]	0.42 [0.36, 0.48]
Lazzerini 2021	12	294	49	1195	Children (< 18y)	0.20 [0.11, 0.32]	0.80 [0.78, 0.82]

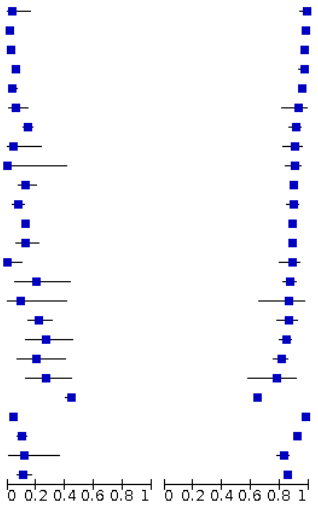
Palpitations (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Feng 2021	0	3	7	122	Adults (≥ 18y)	0.00 [0.00, 0.41]	0.98 [0.93, 1.00]

Figure 27. Forest plot of gastrointestinal signs/symptoms (retrospective data collection)

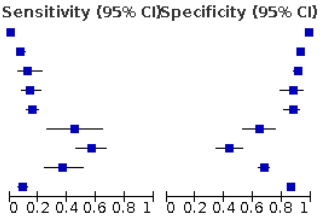
Diarrhoea (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Zhu 2020	1	1	31	83	Adults (≥ 18y)	0.03 [0.00, 0.16]	0.99 [0.94, 1.00]
Wei 2020	12	6	616	302	Adults (≥ 18y)	0.02 [0.01, 0.03]	0.98 [0.96, 0.99]
King 2020	57	13	1930	463	Adults (≥ 18y)	0.03 [0.02, 0.04]	0.97 [0.95, 0.99]
Huang 2020	19	4	317	135	Adults (≥ 18y)	0.06 [0.03, 0.09]	0.97 [0.93, 0.99]
Mao 2020	6	37	182	779	Adults (≥ 18y)	0.03 [0.01, 0.07]	0.95 [0.94, 0.97]
Cunarro-Lopez 2020	4	3	64	40	Adults (≥ 18y)	0.06 [0.02, 0.14]	0.93 [0.81, 0.99]
Martín-Sánchez 2020	62	21	378	206	Adults (≥ 18y)	0.14 [0.11, 0.18]	0.91 [0.86, 0.94]
Xie 2020	1	8	20	76	Adults (≥ 18y)	0.05 [0.00, 0.24]	0.90 [0.82, 0.96]
Feng 2021	0	12	7	113	Adults (≥ 18y)	0.00 [0.00, 0.41]	0.90 [0.84, 0.95]
Ahmed 2021	16	175	107	1523	Adults (≥ 18y)	0.13 [0.08, 0.20]	0.90 [0.88, 0.91]
Arslan 2021	13	25	163	203	Adults (≥ 18y)	0.07 [0.04, 0.12]	0.89 [0.84, 0.93]
Barbhaya 2021	106	182	740	1443	Adults (≥ 18y)	0.13 [0.10, 0.15]	0.89 [0.87, 0.90]
Leung 2021	11	136	75	1036	Adults (≥ 18y)	0.13 [0.07, 0.22]	0.88 [0.86, 0.90]
Fiel-Ozores 2021	0	11	33	82	Adults (≥ 18y)	0.00 [0.00, 0.11]	0.88 [0.80, 0.94]
Haliga 2021	4	30	16	203	Adults (≥ 18y)	0.20 [0.06, 0.44]	0.87 [0.82, 0.91]
Cheng 2020	1	3	10	19	Adults (≥ 18y)	0.09 [0.00, 0.41]	0.86 [0.65, 0.97]
Tordjman 2020	22	14	78	86	Adults (≥ 18y)	0.22 [0.14, 0.31]	0.86 [0.78, 0.92]
Shah 2020	9	45	24	238	Adults (≥ 18y)	0.27 [0.13, 0.46]	0.84 [0.79, 0.88]
Ide 2021	5	48	20	204	Adults (≥ 18y)	0.20 [0.07, 0.41]	0.81 [0.76, 0.86]
Arenas 2020	9	6	25	21	Adults (≥ 18y)	0.26 [0.13, 0.44]	0.78 [0.58, 0.91]
Chung 2021	403	1456	513	2589	Adults (≥ 18y)	0.44 [0.41, 0.47]	0.64 [0.63, 0.65]
Raberahona 2020	61	49	1227	1817	All ages	0.05 [0.04, 0.06]	0.97 [0.97, 0.98]
Vilke 2020	34	558	296	6006	All ages	0.10 [0.07, 0.14]	0.91 [0.91, 0.92]
Sonoda 2021	2	60	15	283	All ages	0.12 [0.01, 0.36]	0.83 [0.78, 0.86]
Lazzerini 2021	18	293	141	1696	Children (< 18y)	0.11 [0.07, 0.17]	0.85 [0.84, 0.87]



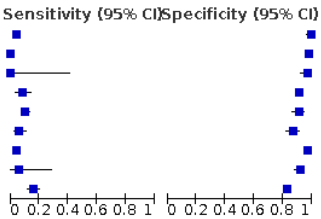
Gastrointestinal symptoms not specified (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Nitecki 2021	17	322	1321	22702	Adults (≥ 18y)	0.01 [0.01, 0.02]	0.99 [0.98, 0.99]
Aldobyany 2020	26	84	314	1011	Adults (≥ 18y)	0.08 [0.05, 0.11]	0.92 [0.91, 0.94]
Hüfner 2020	9	59	61	575	Adults (≥ 18y)	0.13 [0.06, 0.23]	0.91 [0.88, 0.93]
Langer 2020	18	9	106	66	Adults (≥ 18y)	0.15 [0.09, 0.22]	0.88 [0.78, 0.94]
Tan 2021	45	23	242	159	Adults (≥ 18y)	0.16 [0.12, 0.20]	0.87 [0.82, 0.92]
Vieceli 2020	13	25	16	46	Adults (≥ 18y)	0.45 [0.26, 0.64]	0.65 [0.53, 0.76]
Zayet 2020a	54	69	41	53	Adults (≥ 18y)	0.57 [0.46, 0.67]	0.43 [0.34, 0.53]
Sun 2020	20	238	34	496	All ages	0.37 [0.24, 0.51]	0.68 [0.64, 0.71]
Simpson 2020	35	115	343	717	Children (< 18y)	0.09 [0.07, 0.13]	0.86 [0.84, 0.88]



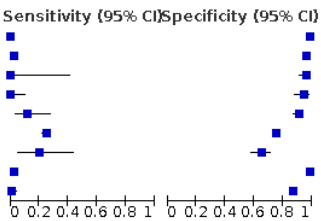
Nausea or vomiting (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	14	1	322	138	Adults (≥ 18y)	0.04 [0.02, 0.07]	0.99 [0.96, 1.00]
Mao 2020	1	16	187	800	Adults (≥ 18y)	0.01 [0.00, 0.03]	0.98 [0.97, 0.99]
Feng 2021	0	4	7	121	Adults (≥ 18y)	0.00 [0.00, 0.41]	0.97 [0.92, 0.99]
Ahmed 2021	10	151	113	1547	Adults (≥ 18y)	0.08 [0.04, 0.14]	0.91 [0.90, 0.92]
Martín-Sánchez 2020	45	21	395	206	Adults (≥ 18y)	0.10 [0.08, 0.13]	0.91 [0.86, 0.94]
Arslan 2021	11	30	165	198	Adults (≥ 18y)	0.06 [0.03, 0.11]	0.87 [0.82, 0.91]
Raberahona 2020	53	54	1235	1812	All ages	0.04 [0.03, 0.05]	0.97 [0.96, 0.98]
Sonoda 2021	1	29	16	314	All ages	0.06 [0.00, 0.29]	0.92 [0.88, 0.94]
Vilke 2020	52	1108	278	5456	All ages	0.16 [0.12, 0.20]	0.83 [0.82, 0.84]



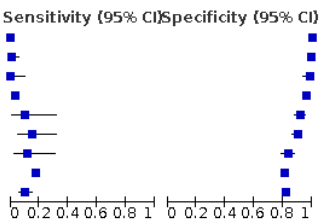
Abdominal pain (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Mao 2020	0	11	188	805	Adults (≥ 18y)	0.00 [0.00, 0.02]	0.99 [0.98, 0.99]
Barbhaya 2021	24	62	822	1563	Adults (≥ 18y)	0.03 [0.02, 0.04]	0.96 [0.95, 0.97]
Feng 2021	0	5	7	120	Adults (≥ 18y)	0.00 [0.00, 0.41]	0.96 [0.91, 0.99]
Fiel-Ozores 2021	0	5	33	88	Adults (≥ 18y)	0.00 [0.00, 0.11]	0.95 [0.88, 0.98]
Shah 2020	4	26	29	257	Adults (≥ 18y)	0.12 [0.03, 0.28]	0.91 [0.87, 0.94]
Chung 2021	229	1011	687	3034	Adults (≥ 18y)	0.25 [0.22, 0.28]	0.75 [0.74, 0.76]
Haliga 2021	4	82	16	151	Adults (≥ 18y)	0.20 [0.06, 0.44]	0.65 [0.58, 0.71]
Raberahona 2020	32	26	1256	1840	All ages	0.02 [0.02, 0.03]	0.99 [0.98, 0.99]
Lazzerini 2021	2	269	157	1720	Children (< 18y)	0.01 [0.00, 0.04]	0.86 [0.85, 0.88]



Vomiting (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	1	0	627	308	Adults (≥ 18y)	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]
Leung 2021	1	12	85	1160	Adults (≥ 18y)	0.01 [0.00, 0.06]	0.99 [0.98, 0.99]
Fiel-Ozores 2021	0	1	33	92	Adults (≥ 18y)	0.00 [0.00, 0.11]	0.99 [0.94, 1.00]
Barbhaya 2021	32	63	814	1562	Adults (≥ 18y)	0.04 [0.03, 0.05]	0.96 [0.95, 0.97]
Haliga 2021	2	19	18	214	Adults (≥ 18y)	0.10 [0.01, 0.32]	0.92 [0.88, 0.95]
Shah 2020	5	28	28	255	Adults (≥ 18y)	0.15 [0.05, 0.32]	0.90 [0.86, 0.93]
Ide 2021	3	41	22	211	Adults (≥ 18y)	0.12 [0.03, 0.31]	0.84 [0.79, 0.88]
Chung 2021	165	769	751	3276	Adults (≥ 18y)	0.18 [0.16, 0.21]	0.81 [0.80, 0.82]
Lazzerini 2021	16	365	143	1624	Children (< 18y)	0.10 [0.06, 0.16]	0.82 [0.80, 0.83]



Loss of appetite (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	3	10	17	223	Adults (≥ 18y)	0.15 [0.03, 0.38]	0.96 [0.92, 0.98]

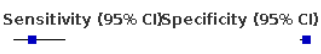
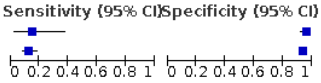


Figure 27. (Continued)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	3	10	17	223	Adults (≥ 18y)	0.15 [0.03, 0.38]	0.96 [0.92, 0.98]
Mao 2020	24	55	164	761	Adults (≥ 18y)	0.13 [0.08, 0.18]	0.93 [0.91, 0.95]



Stomach ache (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	6	2	330	137	Adults (≥ 18y)	0.02 [0.01, 0.04]	0.99 [0.95, 1.00]
Sonoda 2021	1	37	16	306	All ages	0.06 [0.00, 0.29]	0.89 [0.85, 0.92]

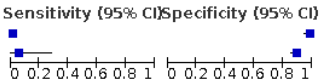
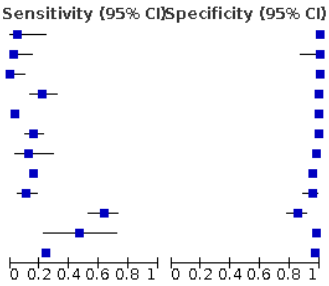


Figure 28. Forest plot of olfactory signs/symptoms (retrospective data collection)

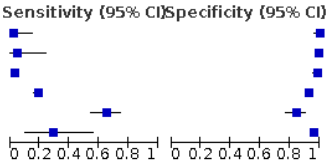
Anosmia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	1	0	19	233	Adults (≥ 18y)	0.05 [0.00, 0.25]	1.00 [0.98, 1.00]
Arenas 2020	1	0	33	27	Adults (≥ 18y)	0.03 [0.00, 0.15]	1.00 [0.87, 1.00]
Chew 2021	0	1	33	704	Adults (≥ 18y)	0.00 [0.00, 0.11]	1.00 [0.99, 1.00]
Leung 2021	19	3	67	1169	Adults (≥ 18y)	0.22 [0.14, 0.32]	1.00 [0.99, 1.00]
Martín-Sánchez 2020	14	2	426	225	Adults (≥ 18y)	0.03 [0.02, 0.05]	0.99 [0.97, 1.00]
Sacks 2020	25	15	132	1575	Adults (≥ 18y)	0.16 [0.11, 0.23]	0.99 [0.98, 0.99]
Chua 2020	4	14	27	672	Adults (≥ 18y)	0.13 [0.04, 0.30]	0.98 [0.97, 0.99]
Barbhaya 2021	139	79	707	1546	Adults (≥ 18y)	0.16 [0.14, 0.19]	0.95 [0.94, 0.96]
Tordjman 2020	11	5	89	95	Adults (≥ 18y)	0.11 [0.06, 0.19]	0.95 [0.89, 0.98]
Zayet 2020a	60	18	35	104	Adults (≥ 18y)	0.63 [0.53, 0.73]	0.85 [0.78, 0.91]
Sonoda 2021	8	9	9	334	All ages	0.47 [0.23, 0.72]	0.97 [0.95, 0.99]
Raberahona 2020	311	63	977	1803	All ages	0.24 [0.22, 0.27]	0.97 [0.96, 0.97]



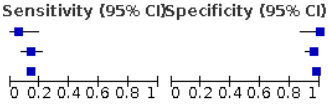
Dysgeusia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	1	0	32	93	Adults (≥ 18y)	0.03 [0.00, 0.16]	1.00 [0.96, 1.00]
Haliga 2021	1	1	19	232	Adults (≥ 18y)	0.05 [0.00, 0.25]	1.00 [0.98, 1.00]
Martín-Sánchez 2020	15	4	425	223	Adults (≥ 18y)	0.03 [0.02, 0.06]	0.98 [0.96, 1.00]
Barbhaya 2021	161	112	685	1513	Adults (≥ 18y)	0.19 [0.16, 0.22]	0.93 [0.92, 0.94]
Zayet 2020a	62	19	33	103	Adults (≥ 18y)	0.65 [0.55, 0.75]	0.84 [0.77, 0.90]
Sonoda 2021	5	13	12	330	All ages	0.29 [0.10, 0.56]	0.96 [0.94, 0.98]



Ageusia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Arenas 2020	2	0	32	27	Adults (≥ 18y)	0.06 [0.01, 0.20]	1.00 [0.87, 1.00]
Tordjman 2020	14	4	86	96	Adults (≥ 18y)	0.14 [0.08, 0.22]	0.96 [0.90, 0.99]
Raberahona 2020	185	38	1103	1828	All ages	0.14 [0.12, 0.16]	0.98 [0.97, 0.99]



Hyposmia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Chua 2020	3	8	28	678	Adults (≥ 18y)	0.10 [0.02, 0.26]	0.99 [0.98, 0.99]

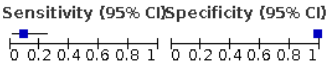
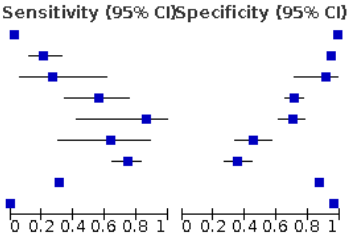


Figure 29. Forest plot of combinations of signs/symptoms (retrospective data collection)

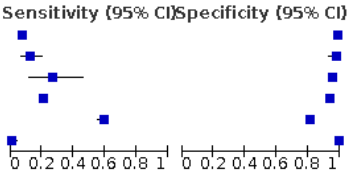
Myalgia or arthralgia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
King 2020	56	8	1931	468	Adults (≥ 18y)	0.03 [0.02, 0.04]	0.98 [0.97, 0.99]
Hüfner 2020	14	34	52	564	Adults (≥ 18y)	0.21 [0.12, 0.33]	0.94 [0.92, 0.96]
Cheng 2020	3	2	8	20	Adults (≥ 18y)	0.27 [0.06, 0.61]	0.91 [0.71, 0.99]
Ide 2021	14	72	11	180	Adults (≥ 18y)	0.56 [0.35, 0.76]	0.71 [0.65, 0.77]
Feng 2021	6	37	1	88	Adults (≥ 18y)	0.86 [0.42, 1.00]	0.70 [0.62, 0.78]
Peng 2020	7	41	4	34	Adults (≥ 18y)	0.64 [0.31, 0.89]	0.45 [0.34, 0.57]
Zayet 2020a	71	79	24	43	Adults (≥ 18y)	0.75 [0.65, 0.83]	0.35 [0.27, 0.44]
Raberahona 2020	398	240	890	1626	All ages	0.31 [0.28, 0.34]	0.87 [0.86, 0.89]
Lazzerini 2021	0	71	159	1918	Children (< 18y)	0.00 [0.00, 0.02]	0.96 [0.96, 0.97]



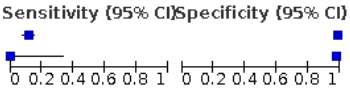
Anosmia or ageusia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
King 2020	153	5	1834	471	Adults (≥ 18y)	0.08 [0.07, 0.09]	0.99 [0.98, 1.00]
Arslan 2021	15	2	103	93	Adults (≥ 18y)	0.13 [0.07, 0.20]	0.98 [0.93, 1.00]
Hüfner 2020	8	23	22	434	Adults (≥ 18y)	0.27 [0.12, 0.46]	0.95 [0.93, 0.97]
Nitecki 2021	284	1451	1054	21573	Adults (≥ 18y)	0.21 [0.19, 0.24]	0.94 [0.93, 0.94]
Chung 2021	502	618	348	2634	Adults (≥ 18y)	0.59 [0.56, 0.62]	0.81 [0.80, 0.82]
Lazzerini 2021	2	10	157	1979	Children (< 18y)	0.01 [0.00, 0.04]	0.99 [0.99, 1.00]



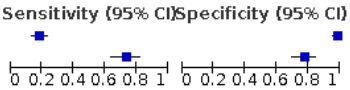
Anosmia/dysosmia or ageusia/dysgeusia (retrospective data collection))

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	38	109	292	6455	All ages	0.12 [0.08, 0.15]	0.98 [0.98, 0.99]
Zurl 2021	0	16	9	603	Children (< 18y)	0.00 [0.00, 0.34]	0.97 [0.96, 0.99]



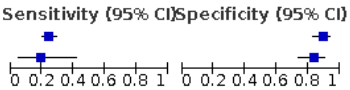
Anosmia or dysgeusia (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Tan 2021	53	3	234	179	Adults (≥ 18y)	0.18 [0.14, 0.23]	0.98 [0.95, 1.00]
Zayet 2020a	70	27	25	95	Adults (≥ 18y)	0.74 [0.64, 0.82]	0.78 [0.69, 0.85]



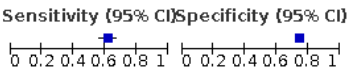
Weakness or fatigue (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	83	15	253	124	Adults (≥ 18y)	0.25 [0.20, 0.30]	0.89 [0.83, 0.94]
Xie 2020	4	14	17	70	Adults (≥ 18y)	0.19 [0.05, 0.42]	0.83 [0.74, 0.91]



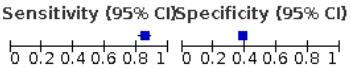
Objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	203	1679	127	4885	All ages	0.62 [0.56, 0.67]	0.74 [0.73, 0.75]



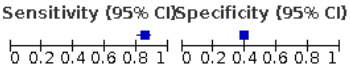
Body aches or fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	282	4045	48	2519	All ages	0.85 [0.81, 0.89]	0.38 [0.37, 0.40]



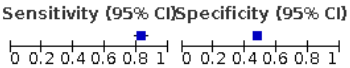
Fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	280	4001	50	2563	All ages	0.85 [0.81, 0.89]	0.39 [0.38, 0.40]



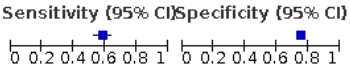
Dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	274	3430	56	3134	All ages	0.83 [0.79, 0.87]	0.48 [0.47, 0.49]



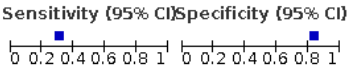
Recent fever or chills (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	193	1608	137	4956	All ages	0.58 [0.53, 0.64]	0.76 [0.74, 0.77]



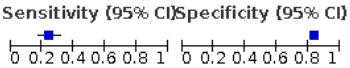
Malaise or fatigue (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Raberahona 2020	403	303	885	1563	All ages	0.31 [0.29, 0.34]	0.84 [0.82, 0.85]



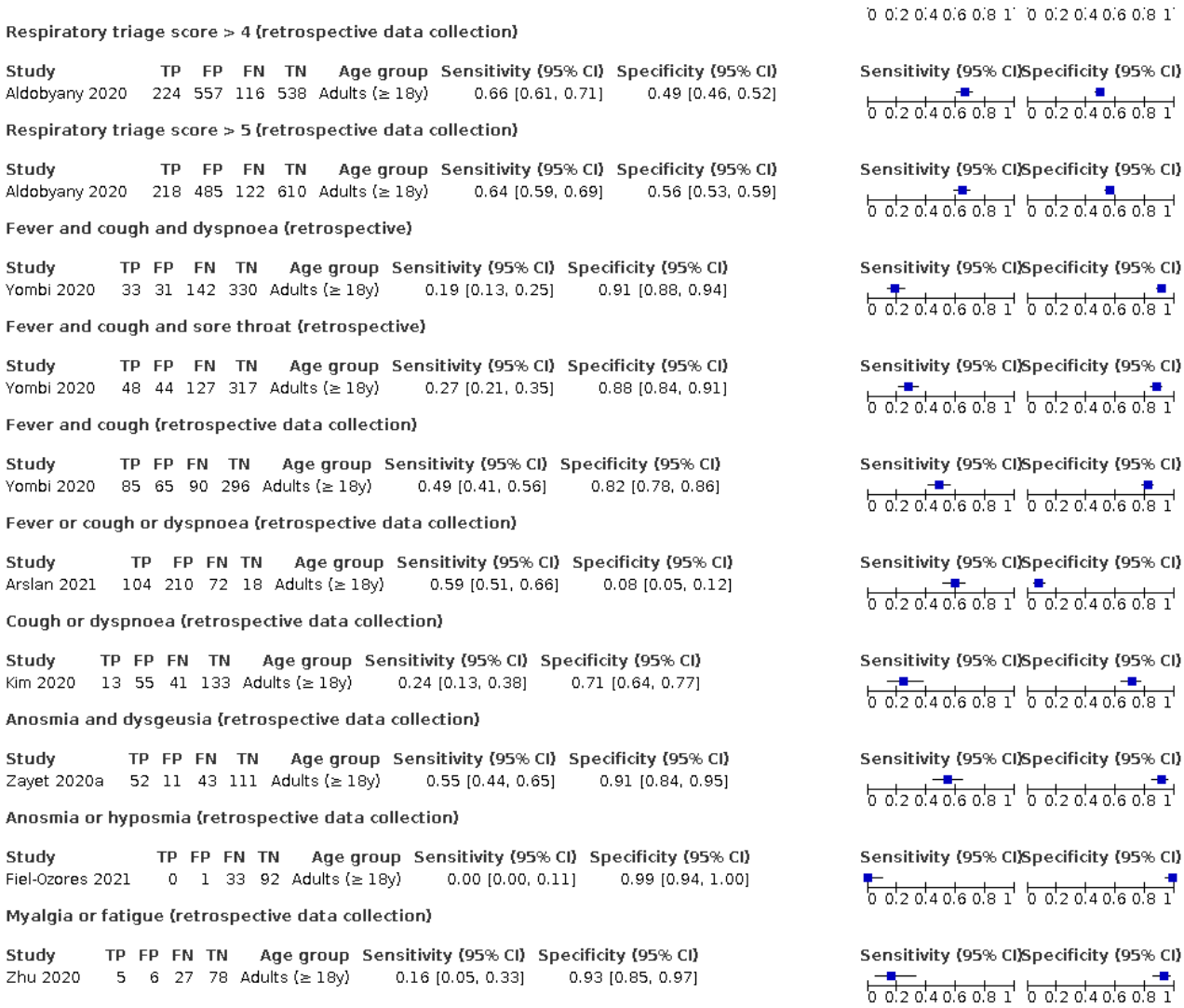
Nausea or vomiting or diarrhoea (retrospective data collection)

Study	TP	FP	FN	TN	Age group	Sensitivity (95% CI)	Specificity (95% CI)
Sacks 2020	38	258	119	1332	Adults (≥ 18y)	0.24 [0.18, 0.32]	0.84 [0.82, 0.86]



Respiratory triage score ≥ 4 (retrospective data collection)

Figure 29. (Continued)



DISCUSSION

Summary of main results

This is the second update of a living systematic review of signs and symptoms for the diagnosis of COVID-19 in an outpatient setting. For the first time, this update provided a large number of cross-sectional studies using prospective data collection, leading to results that are more reliable than those presented in previous versions of this review. Nevertheless, considerable heterogeneity between study results remains a concern. Our main conclusion remains unchanged: most individual symptoms appear to have poor diagnostic accuracy. Neither absence nor presence of symptoms are accurate enough to rule in or rule out the disease. The presence of anosmia or ageusia may be useful as a red flag for the presence of COVID-19. Some combinations of signs and symptoms may be useful as a tool to triage patients for further testing.

This review update identified more studies on combinations of signs and symptoms, but only six out of 29 different combinations were assessed by more than one study. Some combinations may be useful as a triage tool. For example, in a cohort with a disease prevalence (pre-test probability) of 5%, the presence of either anosmia or ageusia would increase the post-test probability of the presence of COVID-19 to 21%.

The combination of signs and symptoms with other readily available information may prove useful in safely ruling out COVID-19. The multivariable prediction score with the highest sensitivity (90.0%) combined gender, being a healthcare worker, recent contact with a COVID-19 case, recent travel, 0.5 times the recent local case detection rate, the presence of rhinorrhoea, cough or dyspnoea, and a combination of age and the presence of fever (SCRiPS Score, Van Walraven 2021). This type of score may be especially useful to safely rule out COVID-19, because it achieves a sensitivity that cannot be obtained by combining symptoms alone. For example, using this score, a 35-year old female healthcare worker without chest symptoms but with fever and rhinorrhoea,

who did not have contact with a COVID-19 case recently and who did not travel recently, would have a 1% chance of having COVID-19 if the local recent case detection rate was 5%. An 85-year old man with fever, without any other symptom, who did not travel recently but who did have a recent contact with a COVID-19 case, would have a 46% chance of having COVID-19 at the same local recent case detection rate of 5%. Of course, such a score should ideally be validated externally in other populations before being applied in practice.

The presence of upper respiratory symptoms such as a sore throat, rhinorrhoea or coryza, increases the probability of having an infectious disease other than COVID-19. In a hypothetical cohort of 1000 individuals, at a COVID-19 prevalence of 5%, 16 people with a sore throat would have COVID-19 and there would be 362 people with a sore throat without COVID-19 (false positives). Not using sore throat as an indication to test wouldn't necessarily lead to 16 people with COVID-19 being missed, as some of those individuals would present with other symptoms that would prompt further testing. We found similar figures for rhinorrhoea and coryza. There is currently no evidence to support further testing in all individuals presenting only with upper respiratory symptoms.

Selection bias is present when selective and non-random inclusion and exclusion of patients apply and the resulting association between exposure and outcome (here the accuracy of the test) differs in the selected study population compared to the eligible study population (Rutjes 2006). For the diagnosis of COVID-19, rapidly and constantly changing and widely variable test criteria have influenced who was referred for testing and who was not, both for the presence of infection and disease. Selection in the study of only a fraction of the eligible patients can result in a biased estimate of the true accuracy of the index test when measured against the reference standard and true disease status. Griffith 2020 have reported on the problematic presence of collider stratification bias in the published studies on COVID-19. Appropriate sampling strategies need to be applied to avoid conclusions of spurious relationships, more specific in our case the biased accuracy estimates of signs and symptoms for the diagnosis of both SARS-CoV-2 infection and COVID-19 disease. Selection of patients based on the presence of specific preset symptoms, such as fever and cough, leads to biased associations between these symptoms and to disease and diagnostic accuracy estimates that differ from their true values. The example of collider bias for cough is illustrated in Figure 30. Grouping studies by diagnostic criteria for selection might clarify this issue, but studies do not clearly describe them, with study authors referring to the guidelines in general that were applicable at the time.

Figure 30. Collider bias

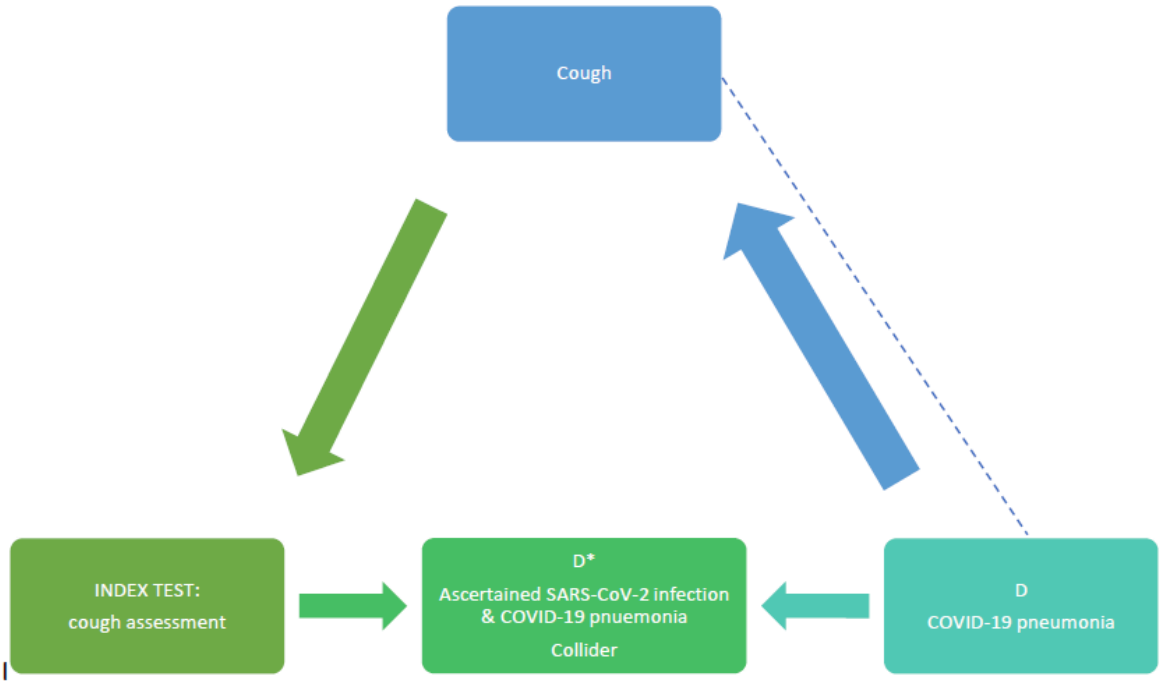


Figure Directed Acyclic Graph (DAG): the symptom, 'cough' is used to enter the study for cough assessment. Both cough and COVID-19 pneumonia (D) result in ascertained diagnosis of SARS-CoV-2 infection (D*). D* is a collider on the pathway between cough and COVID-19 pneumonia leading to a biased association between the symptom cough and COVID-19 pneumonia.

Another form of selection bias is spectrum bias, where the patients included in the studies do not reflect the patient spectrum the index test will be applied to. The inclusion of hospitalised patients can lead to such a bias, when the distribution of signs and symptoms differ in these patients and assessment with the reference standard is differential. In addition, the distribution and severity of

alternative diagnoses may be different in hospitalised populations than in patients presenting to ambulatory care settings. By focusing on prospective studies, spectrum bias was minimised in this review update, as all but two studies, that were performed in a mix of in- and outpatients from paediatric hospitals (Pokorska-Śpiewak 2021; Yonker 2020), were conducted in an outpatient setting.

The observed better sensitivity for cough (and lower specificity) compared to other index tests is unsurprising considering cough was a key feature of COVID-19 that was used in selecting patients for further testing in included studies. As a result, a large proportion of patients in these studies would have a cough, both cases and non-cases. The same applies to fever, for which we observed a large heterogeneity between studies. Some of this heterogeneity was reduced by selecting only studies with a low risk of bias in participant selection for the analyses, but a residual selection bias remained due to preselection based on the presence of fever. The way fever was determined (measured at presentation or self-reported by the patient) and the use of different cut-off levels for fever also contributed to this residual heterogeneity.

Strengths and weaknesses of the review

Strengths of our review are the systematic and broad search performed to include all possible studies, to gather the largest number of peer-reviewed studies available at this point. Exclusion of retrospective studies, the largest number of the published cohorts of patients with COVID-19, from the data analyses limits the available data but improves the quality of the evidence.

The greatest weakness of the review is the risk of selection bias, as discussed above, with many studies selecting their participants based on the presence of fever or respiratory symptoms. Since individuals may or may not be tested on the basis of symptomatic presentation, this limitation is difficult to avoid completely.

Although we included all studies published until June 2021, all studies reported data from 2020 and over 90% of these data were collected in the first half of 2020. Consequently, no studies reported signs or symptoms of specific viral variants.

We need to assess multiple variables for their possible confounding effect on the summary estimates. Possible confounders include the presence of other respiratory pathogens (seasonality), the phase of the epidemic, exposure to high- versus low-prevalence setting, high or low exposure risk, comorbidity of the participants, or time since infection. Seasonality may influence specificity, because alternative diagnoses such as influenza or other respiratory viruses are more prevalent in winter, leading to more non-COVID-19 patients displaying symptoms such as cough or fever, decreasing specificity. In this version of the review, most studies were conducted during the winter or early spring seasons, suggesting this may still have been at play. However, social distancing policies have shortened this year's influenza season in several countries (who.int/influenza/surveillance_monitoring/updates), which may have led to higher specificity for signs and symptoms than what we may expect in the next influenza season. In future updates of the review, we will explore seasonality effects if data allow. As for time since onset, given that the moment of infection is more likely than not an unrecognisable and unmeasurable variable, time since onset of symptoms can be used as a proxy. Reporting of studies, with presentation of the 2x2 table stratified by time since onset of disease, is informative and might have the potential to increase accuracy of the signs and symptoms and their diagnostic differential potential.

Applicability of findings to the review question

In comparison with previous updates, in which many studies included patients who had already been admitted to hospital or who presented to hospital settings with the intent to hospitalise, selection bias was reduced by focusing on prospective studies only. These studies were primarily conducted in outpatient settings, improving the applicability of our findings in comparison with previous review versions.

This review identified only three studies in children. The differences in diagnostic accuracy with adults depended on the type of symptom. The sensitivity of fever in children was higher than the summary estimate across all ages and its specificity was lower. Fever was much more common in children than in adults (higher positivity rate), but often indicated the presence of an infectious disease other than COVID-19 (high proportion of false positives). In contrast, we observed lower sensitivity and higher specificity for fatigue, headache and myalgia in children than in the population as a whole. Olfactory symptoms were investigated by very few studies in children.

Children have been disproportionally underrepresented in studies concerning the diagnosis of SARS-CoV-2 infection. Their absence seems related to the general mild presentation of the disease in the paediatric population and even more frequently the complete asymptomatic course. The full scope of disease presentation in children is however not known. It is important to identify signs and symptoms that can be used to clinically assess children with suspected SARS-CoV-2 infection, especially because non-specific presentations and fever without a source are already common in this age group. Children present as a heterogeneous group, having separate data for neonates, young infants, toddlers, school-aged children and adolescents is of value. Misclassification of children both at their presentation to the healthcare system and in the short term, where children will be asked to remain in quarantine when they present with predefined, but not yet evidence-based symptoms needs to be avoided to decrease the possible damage done to children's health.

Another important patient group that has been neglected in the literature is older adults. They are most at risk of a negative outcome of SARS-CoV-2 infection, especially mortality but also intensive care support. In this version of the review, only two overlapping studies (1 dataset) focused on adults aged 65 years or older. All other studies included adults of all ages and did not present results separately for the older age groups. The lack of a solid evidence base for the diagnosis of COVID-19 in older adults adds to the difficulty in diagnosing serious infections in this age group, in whom other serious infections such as bacterial pneumonia or urinary sepsis also tend to lead to non-specific presentations.

Studies specifically focusing on older adults or children may also enable us to estimate any difference in the diagnostic accuracy of signs and symptoms within these age groups. Given the distinct biological characteristics of children versus younger and versus older adults, these accuracy estimates are likely to be different in different age groups. The current presentation of overall summary estimates may therefore prove too simplistic.

AUTHORS' CONCLUSIONS

Implications for practice

The presence of some signs and symptoms may increase the probability of COVID-19 to an extent that is clinically relevant. Within the context of selection bias in most of the studies in this review, the presence of fever, cough, or anosmia/ageusia should be a reason for further testing for COVID-19.

Other symptoms, such as sore throat, rhinorrhoea or coryza, increase the probability of COVID-19 to a much lesser extent. Selecting patients for reverse transcription polymerase chain reaction (RT-PCR) testing based on these minor symptoms will result in large numbers of people who need to be tested and low positivity rates, making such testing strategies more cumbersome, expensive and less efficient.

However, if the main goal of a country's testing strategy remains to detect as many SARS-CoV-2-positive individuals as possible, denying further testing to people based on the absence of major (and even minor) symptoms will result in many missed cases.

In short, the diagnostic accuracy of symptoms for COVID-19 is moderate to low and any testing strategy using symptoms as selection mechanism will result in both large numbers of missed cases and large numbers of people requiring testing. Which one of these is minimised, is determined by the goal of COVID-19 testing strategies, that is, controlling the epidemic by isolating every possible case versus identifying those with clinically important disease so that they can be monitored or treated, or both, to optimise their prognosis. The former will require a testing strategy that uses very few symptoms as entry criterion for testing, the latter could focus on more specific symptoms such as fever and anosmia.

Implications for research

Our review update reflects the need for a broader diagnostic approach than looking at signs or symptoms alone. Combinations with other, easy-to-obtain information such as patient demographics, the local case detection rate, recent contact with a SARS-CoV-2-positive patient, travel history of the patient, point-of-care test results, vaccination status, and others, may help safely rule out COVID-19 and should be investigated further. Vaccination leads to a reduced rate of asymptomatic infections (Tande 2022). Whether it also alters the clinical presentation of symptomatic COVID-19 patients is unclear at this time. New variants of the virus might also change the clinical presentation. Given the speed with which these variants emerge, it is difficult to provide up-to-date information from a systematic review regarding the diagnostic value of symptoms for COVID-19.

This review will therefore no longer be updated in its current form. Resources allowing, we will consider updating this review when sufficient studies of high methodological quality examining the combination of signs and symptoms with other clinically relevant information such as contact or travel history, or the local recent case detection rate become available. Another important outcome for future updates would be to investigate whether tests exist that identify people requiring respiratory support (SARS or ARDS) or intensive care.

Studies should report the definition of signs and symptoms more clearly, how they were measured, by whom and when. The measurement of key symptoms such as anosmia and ageusia could benefit from standardisation, including the severity and nature of the loss of smell or taste. Yet such standardisation should not be overly complicated as signs and symptoms will typically be used by frontline clinicians who will incorporate these in their more holistic assessment of the patient, which includes more than just diagnosis of COVID-19.

Future studies should also include a broader spectrum of patients with studies in the primary healthcare setting to properly evaluate the diagnostic accuracy of signs and symptoms in this setting. Studies aimed at screening for SARS-CoV-2 infections should also be included, as an increased need for screening is to be expected with the relaxation of quarantine measures. Finally, data are needed on specific patient groups with comorbidities with a higher risk of complications or serious illness and a greater impact of missing early diagnosis of SARS-CoV-2 infection, and the paediatric and elderly population should be added.

We would like to recommend that authors adhere to the STARD guidelines when reporting new studies on this topic (Bossuyt 2015).

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- The project team (Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MMG, Spijker R, Hooft L, Van den Bruel A, McInnes MDF, Emperador D, Dittrich S)
- The systematic review teams for each review:
  - molecular, antigen, and antibody tests (Adriano A, Beese S, Dretzke J, Ferrante di Ruffano L, Harris I, Price M, Taylor-Phillips S);
  - signs and symptoms (Struyf T, Domen J, Horn S, Lannoy V, Wickramasinghe D, Janssens S, Tans A);
  - routine laboratory markers (Yang B, Langendam M, Ochodo E, Guleid F, Holtman G, Verbakel J, Wang J, Stegeman I);
  - imaging tests (Salameh JP, McGrath TA, van der Pol CB, Frank RA, Prager R, Hare SS, Dennie C, Jenniskens K, Korevaar DA, Cohen JF, Van de Wijgert J, Damen JAAG, Wang J).
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The following people conducted the editorial process for this review update.

- Sign-off Editor (final editorial decision): Michael Brown, Michigan State University College of Human Medicine, USA
- Managing Editor (selected peer reviewers, collated peer-reviewer comments, provided editorial guidance to authors, edited the update): Joey Kwong, Cochrane Evidence Production & Methods Directorate
- Editorial Assistant (conducted editorial policy checks and supported editorial team): Leticia Rodrigues, Cochrane Evidence Production & Methods Directorate
- Copy Editor (copy-editing and production): Denise Mitchell, Cochrane Copy Edit Support
- Peer-reviewers (provided comments and recommended an editorial decision): Brendan Delaney, Imperial College London (clinical review); Lao-Tzu Allan-Blitz, Division Global Health Equity: Department of Medicine, Brigham and Women's Hospital Department of Pediatrics, Boston Children's Hospital (clinical review); Paul Garner, Liverpool School of Tropical Medicine (clinical review)*; Jenny Negus (consumer review); Lynda Ware, Cochrane UK (summary versions review); Gianni Virgili and Tanya Walsh, Cochrane Diagnostic Test Accuracy Reviews Editorial Team (methods review); Robin Featherstone, Cochrane Evidence Production & Methods Directorate (search review). *Paul Garner is a member of Cochrane Infectious Diseases and provided peer-review comments on this update, but was not otherwise involved in the editorial process or decision making. One additional peer reviewer provided clinical peer review but chose not to be publicly acknowledged.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ahmed 2021

Study characteristics

Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to compare demographic characteristics of patients who received positive and negative test

Ahmed 2021 *(Continued)*

	results for SARS-CoV- 2 in a population with higher testing rates than among previously published cohorts **Design**: multicenter cross-sectional cohort study, retrospective data collection **Recruitment**: all patients tested for SARSCoV-2 in the UHealth system during the study period were eligible for this cohort study. For a random subset of patients tested during 10-31 March 2020, symptom data were manually extracted from medical records from 24 h before and 24 h after SARS-CoV-2 testing. Medical records were selected to include at least 20% of patients tested on each day, for a total of 1821 patients. **Sample size:** n = 1821 (123 cases) 2021 **Inclusion criteria**: all patients tested for SARS-CoV-2 in the UHealth system during the study period. Test eligibility required at least 1 of the following symptoms - cough, fever, shortness of breath, or a high risk of exposure given recent travel or contact with a person who tested positive. **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 test. Primarily outpatient settings **Facility controls**: negative SARS-CoV-2 test. Primarily outpatient settings **Country:** Utah, USA **Dates**: 10 March 2020-31 March 2020 **Symptoms and severity**: not specified. Primarily mild to moderate severity **Demographics**: median age cases: 38.2 years controls: 39.6 years. Gender: % female cases: 45.8%, controls: 56.7% (entire cohort) **Exposure history**: previous exposure: 56% of cases, 28% of controls; travel: 45% of cases, 25% of controls
Index tests	• Cough • Fever • Shortness of breath • Lethargy • Myalgia • Headache • Sore throat • Nasal symptoms • Diarrhoea • Nausea/vomiting
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (specimen not specified)
Flow and timing	Time interval not specified
Comparative	
Notes	Funding: supported by the National Institute of Allergy and Infectious Diseases (R01 AI135114 to D.T.L.) and the National Heart, Lung, and Blood Institute (K08 HL13650 to R.U.S.) of the National Institutes of Health; and the Centers for Disease Control and Prevention (5U01CK000555-02 to M.H.S. and 5U01CK000538-03 to M.H.S. and L.T.K.)

Ahmed 2021 *(Continued)*

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Ahmed 2021 *(Continued)*

Did all patients receive the same reference standard?	Unclear
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk

Aldobyany 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to determine the diagnostic performance characteristics of the COVID-19 respiratory triage score **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all participants presenting to a tertiary hospital (presenting to ED or clinic) and tested for COVID-19: participants either self-presenting due to symptoms (> 50%), or active screening of contacts to COVID-19 patients or recently travelled (mostly asymptomatic group) **Sample size:** n = 1435 (340 cases) **Inclusion criteria**: all participants presented to King Abdullah Medical City and tested for COVID-19 **Exclusion criteria**: participants who did not have a documented COVID-19 respiratory triage score, or presented prior to 2 April 2020
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Saudi-Arabia **Dates**: 02 April 2020-12 September 2020 (date of submission article) **Symptoms and severity**: mostly asymptomatic, mild or moderate severity **Demographics**: age: controls mean 39.3 years, cases mean 38.7 years M%/F%: cases 68.5/31.5, controls 55.4/44.6 **Exposure history**: not specified, > 70% of participants were HCW
Index tests	• Saudi CDC COVID-19 respiratory triage score (exposure risks + fever or recent history of fever, cough (new or worsening), shortness of breath (new or worsening), nausea, vomiting, and/or diarrhoea) • Fever • Cough • Dyspnoea • GI symptoms
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal swab)

Aldobyany 2020 *(Continued)*

Flow and timing	Timing not specified
Comparative	
Notes	Setting unclear Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Aldobyany 2020 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Alizadehsani 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of COVID-19 pneumonia; to identify risk factors for disease and mortality **Design**: cross-sectional cohort, prospective data collection **Recruitment**: all patients referred to the imaging department through the ED on suspicion of COVID-19 (with flu-like symptoms) **Sample size:** n = 319 (123 cases) **Inclusion criteria**: patients with flu-like symptoms referred to the imaging department **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** patients with positive findings on lung CT **Facility controls**: patients with negative lung CT **Country:** Iran **Dates**: 01 March 2020-08 April 2020 **Symptoms and severity**: not specified. 1/3 had COVID-19 pneumonia **Demographics**: mean age cases: 52.0 years controls: 44.1 years M%/F%: cases 40.8/59.2, controls 50.4/49.6 **Exposure history**: travelling in past 3 months: cases 4.9%, controls 3.1%
Index tests	• Fever • Dyspnoea • Weakness • Shivering • Fatigue • Dry cough • Anorexia • Anosmia • Ageusia • Dizziness

Alizadehsani 2021 *(Continued)*

	• Sweating
Target condition and reference standard(s)	• TC: COVID-19 pneumonia • RS: thin-slice high-resolution multi-slice spiral CT scan in a supine position, and high-resolution CT images of all patients were reviewed by a radiologist with > 14 years of experience in chest imaging
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	

Alizadehsani 2021 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Allegorico 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to explore the value of lung ultrasonography to predict RT-PCR test results **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** consecutive ED patients were included if they had either fever (body temperature > 37.5 °C) and/or history of cough and/or dyspnoea within the previous 48 h as assessed on day 1 **Sample size:** n = 79 (42 cases) **Inclusion criteria**: all patients with fever (body temperature > 37.5 °C measured using infrared thermometer) and of cough and/or dyspnoea **Exclusion criteria**: patients with missing clinical, biochemistry and radiological data (thoracic ultrasound, CT scan)
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country: Italy** **Dates**: 01 March 2020-30 April 2020 **Symptoms and severity**: not specified. 75% of all participants had dyspnoea **Demographics**: median age cases 68.5 years, controls 67.5 years M%/F%: cases 69.0/31.0, controls 67.6/32.4 **Exposure history**: not specified
Index tests	• Body temperature • Cough • Dyspnoea • Respiratory rate

Allegorico 2020 *(Continued)*

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasal swab)
Flow and timing	Index tests and RS both taken on day 1
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Allegorico 2020 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Arenas 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the clinical features of kidney transplant (KT) and maintenance haemodialysis (MHD) patients, comparing confirmed and suspected non-confirmed COVID-19 cases **Design**: cross-sectional multicenter cohort study, retrospective data collection **Recruitment:** all KT recipients and MHD patients who were studied in the Hospital del Mar for suspected COVID-19 infection **Sample size:** n = 61 (34 cases) **Inclusion criteria**: any patients admitted in that 40-day period with COVID-19-compatible signs, fever was the main symptom leading to suspicion of COVID-19 and testing **Exclusion criteria**: none specified
Patient characteristics and setting	**Definition cases:** all KT and MHD patients admitted with a single positive RT-PCR test for SARS-CoV-2 (1 case with first a negative and later on a positive test) **Definition controls**: negative RT-PCR test for SARS-CoV-2 (17/27 got a consecutive negative test) **Country:** Spain **Dates**: 12 March 2020-21 April 2020 **Symptoms and severity**: inclusion based on potential COVID-symptoms 30/34 cases pneumonia, 5/27 controls had pneumonia **Demographics**: age: controls mean 62.1 years, cases mean 69.0 years M%/F%: cases 70.6/29.4, controls 78.8/21.2 **Exposure history**: not specified
Index tests	• Fever • Cough • Dyspnoea • Asthenia • Myalgia

Arenas 2020 *(Continued)*

	• Diarrhoea • Headache • Ageusia • Anosmia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs or bronchoalveolar lavage
Flow and timing	Unclear time interval. Symptoms recorded on admission. Timing of reference test not specified
Comparative	
Notes	KT and MHD patients: very specific population at higher risk of infection Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		

Arenas 2020 *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Arslan 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to identify the clinical findings and outcomes of children with COVID-19 and factors predicting RT-PCR positivity **Design**: cross-sectional cohort study, retrospective data collection **Recruitment**: all suspected COVID-19 patients (children) admitted to and treated in the ED, inpatient clinic, or paediatric ICU of a tertiary hospital (suspected if a child had contact with a confirmed COVID-19 case, lived in an epidemic area where COVID-19 case(s) were reported, or had any family member hospitalised due to a respiratory infection or experiencing symptoms such as cough, fever, or shortness of breath in the last 2 weeks and if the children had respiratory or GI symptoms) **Sample size:** n = 404 (176 cases) **Inclusion criteria**: children between 1 month and 18 years of age presenting to the ED, inpatient clinic, or paediatric ICU, suspected of COVID-19 **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 test **Facility controls**: negative SARS-CoV-2 test **Country:** Turkey **Dates**: 20 March 2020-31 May 2020 **Symptoms and severity**: asymptomatic: 33.5% of cases; mild: 53.4% of cases; moderate: 12.5% of cases; severe: 0.0% of cases; critical: 0.6% of cases **Demographics**: median age cases 79 months, controls 30.5 months

Arslan 2021 *(Continued)*

	M%/F%: cases 55.7/44.3, controls 59.2/40.8 **Exposure history**: previous exposure to SARS-CoV-2-infected person: cases 93%, controls 23%
Index tests	• Cough • Shortness of breath • Fatigue • Sore throat • Rhinorrhoea • Nausea/vomiting • Diarrhoea • Smell/taste loss • Tachypnoea • Tachycardia • Low oxygen saturation (< 92%) • Crackle • Rhonchus
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal swab)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		

Arslan 2021 *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Barbhaya 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to investigate and characterise mild to moderate COVID-19 and risk factors **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** patients presenting to a dedicated ambulatory COVID-19 clinic in Washington DC **Sample size:** n = 2471 (846) **Inclusion criteria**: patients from the community and hospital associates; PCR tested, prescreened for symptoms or exposure; decisions for testing made according to CDC guidelines in place at the time of each encounter, most often only if the patient was symptomatic **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 test **Facility controls**: negative SARS-CoV-2 test

Barbhaya 2021 *(Continued)*

	Country: USA **Dates**: 11 March 2020-14 June 2020 **Symptoms and severity**: mild to moderate disease 88.9%, severe disease (= hospitalisation) 11.1% **Demographics**: mean age cases 43.2 years, controls 43.5 years M%/F%: cases 47.8/52.0, controls 35.5/64.4, 0.1% not specified **Exposure history**: exposure to patient with COVID-19 58.7%
Index tests	• Anosmia • Subjective fever • Change in taste • Anorexia • Objective fever • Myalgias • Cough • Chills • Fatigue/malaise • Dizziness • Headache • Nausea • Diarrhoea • Rhinorrhoea • Vomiting • Shortness of breath • Chest pain • Abdominal pain • Sore throat • Congestion
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal and mid-turbinate swab)
Flow and timing	Index tests and RS both taken at presentation
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		

Barbhaya 2021 *(Continued)*

Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Bhattacharya 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to evaluate the clinical symptoms among patients with suspected COVID-19 presenting to screening outpatient clinics to develop and validate a clinical symptom-based scoring system **Design**: cross-sectional cohort study, prospective data collection

Bhattacharya 2021 *(Continued)*

	Recruitment: patients presenting to an outpatient clinic at a tertiary care hospital **Sample size:** n = 378 (125) **Inclusion criteria**: patients who were suspected of having COVID-19 and tested, provided informed consent and were contacted successfully by phone, from 1066 suspected patients who were tested during this period, 384 patients were enrolled in the study based on the availability of informed consent and successful telephonic communication). Suspicion was based on the testing advisory developed by the Indian Council of Medical Research (ICMR), Version 5, dated 18 May 2020. "ILI symptoms", defined as acute respiratory infection with fever ≥ 38 °C AND cough. **Exclusion criteria**: no PCR test result
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 test **Facility controls**: negative SARS-CoV-2 test **Country:** India **Dates**: 17 June 2020-1 July 2020 **Symptoms and severity**: not specified, mostly mild to moderate severity **Demographics**: mean age overall 35.6 years M%/F% overall: 65.1/34.9 **Exposure history**: not specified
Index tests	• Body temperature (cutoff fever >37.8°C) • Sore throat • Cough • Headache • Myalgia • Breathlessness • Nausea • Vomiting • Diarrhoea • Loss of smell
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasal + throat swab)
Flow and timing	Index tests and RS both at presentation, phone interview after test was taken but before result was generated
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Bhattacharya 2021 *(Continued)*

Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Unclear risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Unclear risk	

Bouzid 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to identify clinical or biological characteristics to help distinguish SARS-CoV-2 from other respiratory viruses **Design**: cross-sectional cohort study, prospective data collection **Recruitment**: all consecutive patients admitted through the ED and presenting with respiratory symptoms **Sample size:** n = 596 (268 cases) (from 03 March 2020) **Inclusion criteria**: all consecutive patients presenting with an influenza-like illness (ILI: fever with a temperature > 38.5 °C, malaise, headache, and myalgia; and 1 respiratory symptom (cough, sore throat, and dyspnoea)) and admitted to the hospital through the ED **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 test **Facility controls**: negative SARS-CoV-2 test **Country:** France **Dates**: 03 March 2020-30 March 2020 **Symptoms and severity**: not specified, all patients presented with ILI, 13% needed ICU admission, 13% died **Demographics**: median age cases 59 years, controls 62 years M%/F%: cases 71.0/29.0, controls 50.0/50.0 **Exposure history**: not specified
Index tests	• Feverishness • Hypothermia • Chills • Sweats • Headaches • Myalgia • Malaise • Cough • Sore throat • Dyspnea • Expectoration • Chest pain • Bilateral cracklings
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: depending on kit availability, viral investigations were conducted either with the QIAstat-Dx Respiratory SARS-CoV-2 Panel (Qiagen, Hilden, Germany), allowing for the detection of respiratory pathogens plus SARS-CoV-2, or with a combination of the RT-PCR RealStar SARS-CoV-2 Kit RUO (Altona Diagnostics, Hamburg, Germany) and rapid multiplex PCR FilmArray RP2 (BioFire, BioMerieux, Marcy- L'Etoile, France), specimen not specified

Bouzid 2020 *(Continued)*

Flow and timing	Index tests and RS both taken at ED admission
Comparative	
Notes	Conflicts of interest: DB and BV declare having received past personal fees and grant from Qiagen (Hilden, Germany) Funded by the AP-HP (Assistance Publique – Hôpitaux de Paris). This study was supported by Qiagen in the form of a grant funding the data management of the RespiFast2 study targeting to assess the impact of respiratory viruses and of discounted equipment and consumables in the context of the COVID-19 outbreak.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Bouzid 2020 *(Continued)*

Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	No	
Were all patients included in the analysis?	Unclear	
Could the patient flow have introduced bias?		Unclear risk

Brendish 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to examine and compare the clinical characteristics, symptoms, and outcomes of adult patients presenting to the ED or Acute Medicine Unit (AMU), testing positive and negative for COVID-19 **Design**: cross-sectional cohort study, prospective data collection from a large, controlled, non-randomised trial of molecular POC testing vs laboratory RT-PCR for SARS-CoV-2 **Recruitment**: all consecutive patients presenting to the ED or AMU or other admissions area of Southampton, with an acute respiratory illness or otherwise clinically suspected of having COVID-19 (= all patients included in the CoV-19 POC trial) **Sample size:** n = 1054 (352 cases) **Inclusion criteria**: all consecutive adults (≥ 18 years old), presenting to the ED or AMU or other admissions area of Southampton, with an acute respiratory illness or otherwise clinically suspected of having COVID-19 **Exclusion criteria**: not fulfilling all the inclusion criteria; declines nasal/pharyngeal swabbing; consent declined or consultee consent declined; already recruited to the study in the last 14 days
Patient characteristics and setting	**Facility cases:** PCR-positive patients by either molecular POC testing or laboratory RT-PCR **Facility controls**: PCR-negative patients by either molecular POC testing or laboratory RT-PCR **Country:** UK **Dates**: 20 March 2020-29 April 2020 **Symptoms and severity**: mild to moderate to severe • 20% of cases received supplemental oxygen, 10% of controls

Brendish 2020 *(Continued)*

	• 18% of cases admitted to ICU, 6% of controls • 25% of cases died within 30 days, 12% of controls **Demographics**: median age cases 68 years, controls 69 years M%/F%: cases 57.4/42.6, controls 51.7/48.3 **Exposure history**: not specified, 21% of cases a HCW, 5% of controls
Index tests	• Sore throat • Rhinorrhoea • Wheeze • Shortness of breath • Pleuritic chest pain • Cough • Sputum • Fever (body temperature ≥ 37.8 °C) • Chills • Fatigue • Reduced appetite • Headache • Myalgia • Diarrhoea • Abdominal pain • Anosmia • Heart rate • Respiratory rate • Systolic BP
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: either laboratory RT-PCR or molecular POC testing (QIAGEN) for SARS-CoV-2 (nasopharyngeal swab)
Flow and timing	Index tests and RS both taken at admission
Comparative	
Notes	Unclear how decision was made which patients received which RS. Funding: the CoV-19 POC trial was funded by University of Southampton and University Hospital Southampton NHS Foundation Trust. NJB is supported by a National Institute of Health Research (NIHR) Clinical Lecturer post. TWC is supported by a NIHR Fellowship (PDF 2016-09-061).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		

Brendish 2020 *(Continued)*

Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		

Brendish 2020 *(Continued)*

Could the patient flow have introduced bias?	Unclear risk

Buonafine 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to investigate the prevalence and clinical characteristics of HCWs with COVID-19 symptoms **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** HCW from the Santa Casa de São Paulo Hospital were defined as symptomatic and invited to participate in the study if presented with self-reported fever or symptoms suspicious of COVID-19 **Sample size:** n = 295 (125 cases) **Inclusion criteria**: HCW with self-reported fever or any of the following: acute respiratory symptoms (cough, nasal congestion, sore throat, shortness of breath), loss or changed sense of smell or taste, ocular symptoms, headache, arthralgia, myalgia, fatigue, diarrhoea, nausea, and vomiting **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** RT-PCR-positive for SARS-CoV-2 **Facility controls**: RT-PCR-negative for SARS-CoV-2 **Country:** Brazil **Dates**: 21 March 2020-22 May 2020 **Symptoms and severity**: mild to moderate to severe: 7% hospitalised 2% died, 91% of included individuals had headache, 88% nasal congestion, 85% cough, 85% fatigue, 81% myalgia **Demographics**: mean age cases 35 years, controls 34 years M%/F%: cases 40.0/60.0, controls 23.6/76.4 **Exposure history**: all HCW. Close contact with confirmed COVID-19: cases 73%; controls 74%
Index tests	• Headache • Nasal congestion • Cough • Fatigue • Myalgia • Sore throat • Chills • Ocular pain • Fever • Arthralgia • Diarrhoea • Abdominal pain • Shortness of breath

Buonafine 2020 *(Continued)*

	• Cutaneous rash • Anosmia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal and oropharyngeal swab)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Buonafine 2020 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Chan 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all patients aged ≥ 18 years in custody in a New York City jail facility or hospital units housing patients from the jail system who were tested for COVID-19 **Sample size:** n = 721 (510 cases) **Inclusion criteria**: all patients aged ≥ 18 (as of 11 March 2020) in custody in a New York City jail facility or hospital units housing patients from the jail system and tested for COVID-19 **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** RT-PCR positive for SARS-CoV-2 **Facility controls**: RT-PCR negative for SARS-CoV-2 **Country:** New York, USA **Dates**: 11 March 2020-28 April 2020 **Symptoms and severity**: mild to moderate to severe: 8% hospitalised, 1% ICU admission, 1% died **Demographics**: median age cases 37 years, controls 33 years M%/F%: cases 91.0/9.0, controls 92.0/8.0 **Exposure history**: not specified, all participants in custody in the New York City jail system during a COVID-19 outbreak
Index tests	• Cough • Fever • Sore throat • Shortness of breath

Chan 2021 *(Continued)*

	• Myalgia • Malaise • Headache • Fatigue • Chills
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal swab)
Flow and timing	Timing not specified
Comparative	
Notes	Very specific population Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Chan 2021 *(Continued)*

Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
Could the patient flow have introduced bias?		Unclear risk

Cheng 2020

Study characteristics	
Patient Sampling	**Purpose:** to identify the clinical features and CT manifestations of COVID-19 and compare them with those of pneumonia occurring in patients who do not have COVID-19 **Design**: cross-sectional, single-centre, retrospective study **Recruitment:** pneumonia patients who presented at a fever observation department in Shanghai **Sample size:** n = 33 (11 cases) **Inclusion criteria**: patients with clinical and radiological features of pneumonia, and a normal or reduced total leukocyte count or total lymphocyte count, plus an epidemiologic history that included travel or a history of residence in Hubei Province or other areas where continuous transmission of local cases occurred within 14 days before onset of symptoms, a history of contact with patients who had fever or respiratory symptoms and were from Hubei Province or other areas with continuous transmission of local cases within 14 days before onset of the disease, or clustering or epidemiologic association with the new coronavirus infection **Exclusion criteria**: not defined
Patient characteristics and setting	**Facility cases:** confirmed case: positive RT-PCR test result obtained by a throat swab. Test was repeated when the first test was negative **Facility controls**: pneumonia patients confirmed not to be infected by SARS-CoV-2 (2 PCR tests) **Country:** China **Dates**: 19 January 2020-6 February 2020 **Symptoms and severity**: pneumonia was defined as patients with at least 1 clinical symptom (i.e. cough, sputum, fever, dyspnoea, or pleuritic chest pain), a finding of either coarse crackles on auscultation or elevated inflammatory biomarkers, and observation of a new pulmonary opacification on chest CT

Cheng 2020 *(Continued)*

	Demographics: median age ± SD cases 50.36 ± 15.5, controls 43.59 ± 16.02, gender distribution cases (M/F: 8/3), controls (M/F: 7/15) **Exposure history**: cases 8/11, controls 7/22 (in the last 14 days with patients with fever or respiratory symptoms or with known cases)
Index tests	• Fever • Cough • Sputum • Shortness of breath • Muscle ache • Diarrhoea • Sore throat • Peak body temperature
Target condition and reference standard(s)	• TC: COVID-19 pneumonia • RS: RT-PCR testing on throat swab specimens Tests were repeated if the first test was negative
Flow and timing	Time interval not specified, reference test at day 0 (or later when the first test was negative), index tests were questionnaired at day 0 for the presence of symptoms in the past period of time
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		

Cheng 2020 *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Chew 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to develop a prediction model to identify patients who are at low risk of having COVID-19 **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all patients admitted to the Pneumonia and Acute Respiratory Infection (PARI) wards of Changi General Hospital **Sample size:** n = 1228 (52 cases) **Inclusion criteria**: all patients admitted to PARI wards **Exclusion criteria**: none specified, for patients with multiple admissions during the study period, analysis was limited to the first PARI admission

Chew 2021 *(Continued)*

Patient characteristics and setting	**Facility cases:** RT-PCR-positive for SARS-CoV-2 **Facility controls**: RT-PCR-negative for SARS-CoV-2 **Country:** Singapore **Dates**: 10 February 2020-30 April 2020 **Symptoms and severity**: not specified, mild to moderate severity **Demographics**: median age cases 48 years, controls 64 years M%/F%: total cohort 59.9/40.1 **Exposure history**: contact with people with acute respiratory infection, cases 36%, controls 4%; travel history: cases 3%, controls 2%
Index tests	• Fever • Cough • Sore throat • Rhinorrhoea • Anosmia • Breathlessness • Headache • Chest discomfort
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal and oropharyngeal swab)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			

Chew 2021 *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Chua 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to evaluate the utility of acute olfactory loss as a risk- stratifying tool for COVID-19 **Design**: retrospective cohort study **Recruitment:** chart review was performed for all patients who presented with acute respiratory symptoms, and in those who fulfilled the prevailing Ministry of Health suspect or surveillance case definition, at ED of tertiary hospital **Sample size:** n = 688 (24 cases) **Inclusion criteria**: all patients with suspected SARS-CoV-2 infection (suspicion based on presence of acute respiratory symptoms, and fulfilling the prevailing Ministry of Health suspect or surveillance case definition)

Chua 2020 *(Continued)*

	Exclusion criteria: patients with pre-existing olfactory loss, and those who were unable to give a history of olfactory loss reliably (e.g. those with cognitive impairment)
Patient characteristics and setting	**Facility cases:** suspected patients with a positive PCR test **Facility controls**: suspected patients with a negative PCR test **Country:** Singapore **Dates**: 23 March 2020-04 April 2020 **Symptoms and severity**: not specified **Demographics**: age: not specified gender: not specified **Exposure history**: not specified
Index tests	• Hyposmia • Anosmia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (oropharyngeal swab)
Flow and timing	RS and index tests both taken at presentation
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	

Chua 2020 *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Chung 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) - compare symptoms and characteristics of people with and without laboratory-confirmed SARS-CoV-2 infection **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** research staff screened for study eligibility among people of all ages who had sought medical care (e.g. tele health, primary care, urgent care, and EDs) and/or COVID-19 testing for an acute respiratory illness **Sample size:** n = 4961 (916 cases) **Inclusion criteria**: reported acute illness with fever/feverishness, cough, or shortness of breath/difficulty breathing and had a respiratory specimen collected for SARS-CoV-2 testing within 10 days of illness onset **Exclusion criteria**: people tested by antigen detection assays alone; swabbed, tested, or interviewed > 10 days after symptom onset; inconclusive RT-PCR results
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 test **Facility controls**: negative SARS-CoV-2 test **Country:** USA

Chung 2021 *(Continued)*

	Dates: 26 March 2020-15 August 2020 **Symptoms and severity**: not specified, mostly mild to moderate **Demographics**: age groups ≤ 4 years: cases 1% controls 6%; 5-17 years: cases 4% controls 8%; 18-49 years: cases 65% controls 56%; 50-64 years: cases 21% controls 22 years; ≥ 65 years: cases 9% controls 9% M%/F%: cases 61.0/39.0, controls 67.0/33.0 **Exposure history**: previous exposure to person with known COVID-19: cases 59%, controls 18%
Index tests	• Cough • Fever/feverishness • Shortness of breath • Loss sense of taste/smell • Headache • Muscle aches • Nasal congestion • Chills • Sore throat • Diarrhea • Abdominal pain • Vomiting
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasal or nasopharyngeal swab)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: supported through cooperative agreements funded by the US Centers for Disease Control and Prevention and, at the University of Pittsburgh, by infrastructure funding from the National Institutes of Health (UL1 TR001857).

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern

Chung 2021 *(Continued)*

DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		High risk	

Clemency 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to develop symptom-based criteria for screening of HCW for SARS-CoV-2 **Design**: prospective observational cohort **Recruitment:** HCW with symptoms concerning for COVID-19 infection were evaluated for potential testing through a centralised nurse call centre and referred to outpatient drive-through testing sites if any suspicion of infection **Sample size:** n = 961 (225 cases)

Clemency 2020 *(Continued)*

	Inclusion criteria: all HCW tested for SARS-CoV-2, based on symptom-based triage ("symptoms concerning for COVID-19 infection" **Exclusion criteria**: none specified (141 excluded because symptoms were not documented, 12 excluded because test results not available)
Patient characteristics and setting	**Facility cases:** all consecutive HCW with a single positive RT-PCR test for SARS-CoV-2 **Facility controls**: all consecutive HCW with a single negative RT-PCR test for SARS-CoV-2 **Country:** New York, USA **Dates**: 26 March 2020-16 April 2020 **Symptoms and severity**: mild to moderate severity, inclusion based on presenting symptoms **Demographics**: mean age not presented; gender not presented **Exposure history**: not presented (likely a high rate of exposure, because HCW)
Index tests	• Fever • Fatigue • Dry cough • Loss of appetite • Myalgia • Difficulty breathing • Coughing up phlegm • Sore throat • Diarrhoea • Loss of taste or smell
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: (single) RT-PCR, nasopharyngeal or oropharyngeal swabs
Flow and timing	HCW referred for reference test after index test, but exact time interval not specified
Comparative	
Notes	Funding: supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under award UL1TR001412 to the University at Buffalo

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		

Clemency 2020 *(Continued)*

Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Clifford 2020

Study characteristics			

Clifford 2020 *(Continued)*

Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to investigate the association between different triage chief complaints and COVID-19 status **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all adult ED visits (structured data) of patients who underwent nasopharyngeal swab RT-PCR testing **Sample size:** n = 11992 (6524 cases) **Inclusion criteria**: all adult patients undergoing RT-PCR at the ED **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** RT-PCR-positive for SARS-CoV-2 **Facility controls**: RT-PCR-negative for SARS-CoV-2 **Country:** New York, USA **Dates**: 01 March 2020-13 May 2020 **Symptoms and severity**: mild to moderate to severe; hospital admission cases 65% controls 47%; mortality cases 20% controls 4%; intubation and ventilation cases 16% controls 4% **Demographics**: median age cases 62 years, controls 54 years M%/F%: cases 55.5/44.5, controls 48.5/51.5 **Exposure history**: not specified
Index tests	• Fever • Shortness of breath • Cough • Weakness/fall/altered mental status • Endocrine • Other viral symptoms • GI complaints • Genitourinary complaints • Neurological deficit or cerebrovascular accident, stroke-like symptoms, or seizures • Chest pain • Abdominal pain • Orthopedic complaints
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal swab)
Flow and timing	Timing of RS not specified
Comparative	
Notes	Funding: none declared
Methodological quality	

Clifford 2020 *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Cunarro-Lopez 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to examine maternal-perinatal outcomes in pregnant women with suspected COVID-19 according to the result of a RT-PCR test and to investigate possible variables that could be useful for predicting a negative RT-PCR result **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** obstetrics patient (pregnant, in labour or puerperium) with suspected COVID-19 who attended the hospital **Sample size:** n = 111 (68 cases) **Inclusion criteria**: all obstetrics patients (pregnant, in labour or puerperium) with suspected COVID-19 who attended the hospital **Exclusion criteria**: non-conclusive RT-PCR result, those patients who did not undergo obstetric follow-up in the hospital and asymptomatic patients with SARS-CoV-2 infections
Patient characteristics and setting	**Facility cases:** RT-PCR positive for SARS-CoV-2 **Facility controls**: RT-PCR negative for SARS-CoV-2 **Country:** Spain **Dates**: 10 March 2020-12 May 2020 **Symptoms and severity** • cases: mild 52%, moderate 28%, severe 12%, critical 6% • controls: mild 79%, moderate 16%, severe 5%, critical 0% **Demographics**: mean age cases 34 years, controls 32 years M%/F%: cases 0.0/100.0, controls 40.0/100.0 **Exposure history**: not specified
Index tests	• Fever • Cough • Shortness of breath • Diarrhoea • Body temperature • Breathing frequency
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasal or pharyngeal swab)
Flow and timing	Timing of RS not specified
Comparative	
Notes	Funding: by University of Alcalá (COVID-19 UAH 2019/00003/016/001/023) and by (FIS-PI18/00912) the Instituto de Salud Carlos III (Plan Estatal de I

Cunarro-Lopez 2020 *(Continued)*

	+ D+I 2013-2016) and co financed by the European Development Regional Fund

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Cunarro-Lopez 2020 *(Continued)*

Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Drager 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to analyse clinical characteristics of patients with SARS-CoV-2 suspicion **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all symptomatic patients presenting at the Corona outpatient clinic at the Carl Gustav Carus University hospital of Dresden **Sample size:** n = 2257 (163 cases) **Inclusion criteria**: all patients presenting themselves at the outpatient clinic: patients with symptoms (not further specified) + high-risk contacts or returning from a high-risk area where tested for SARS-CoV-2 **Exclusion criteria**: non specified
Patient characteristics and setting	**Facility cases:** RT-PCR-positive for SARS-CoV-2 **Facility controls**: RT-PCR-negative for SARS-CoV-2 **Country:** Germany **Dates**: 09 March 2020-31 March 2020 **Symptoms and severity**: mostly cough and upper airway symptoms, mild to moderate, no hospitalisations specified **Demographics**: median age overall 39 years overall 45% male 55% female 32% had pre-existing Illness **Exposure history**: 5% tested based on epidemiology (returning from high-risk area), 27% had exposure to COVID-19-positive patient(s)
Index tests	• Cough • Headache • Nasal congestion • Muscle pains • Sore throat • Fever • Diarrhoea • Shortness of breath

Drager 2020 *(Continued)*

	• Vomiting/nausea
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: not specified (throat swab)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear

Drager 2020 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Feng 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of COVID-19 pneumonia **Design**: cross-sectional, retrospective, single-centre study **Recruitment:** patients admitted to ED with history of exposure to COVID-19 **Sample size:** n = 132 (cases = 7) **inclusion criteria**: all patients admitted to the fever clinic of the ED of the First Medical Center, Chinese People's Liberation Army General Hospital (PLAGH) in Beijing with the epidemiological history of exposure to COVID-19 according to WHO interim guidance **Exclusion criteria**: < 14 years old, no other criteria specified
Patient characteristics and setting	**Facility cases:** among clinically suspected patients: those with a positive RT-PCR **Facility controls**: clinically non-suspected patients + suspected patients with negative RT-PCR **Country:** China **Dates**: 14 January 2020-9 February 2020 **Symptoms and severity**: all patients admitted, with exposure history to COVID-19, so all levels of severity; days from illness onset until admission (median, IQR): 2.0 (1.0-5.0); patient population with general mild disease and limited presence of comorbidities (range 0%-2.3% (COPD)) **Demographics**: age: controls median 40.0 years (IQR 32.5-54.5), cases median 39.0 years (IQR 37.0-41.5) M%/F%: cases 71.4/28.6, controls 63.2/36.8 **Exposure history**: epidemiological history of exposure to COVID-19 (as per WHO guidance)
Index tests	• Heart rate • Diastolic BP • Systolic BP • Fever (former: median only on all and cases - no control median given) • Highest temperature • Cough

Feng 2021 *(Continued)*

	• Shortness of breath • Muscle ache • Headache • Sore throat • Rhinorrhoea • Diarrhoea • Nausea • Vomiting • Chills • Shiver • Expectoration • Abdominal pain • Fatigue • Palpitation
Target condition and reference standard(s)	• TC: COVID-19 pneumonia • RS: in-house RT-PCR (E-gene) - at 4 institutions
Flow and timing	Index test and RS both taken on admission
Comparative	
Notes	Funding: supported by grants from the PLA Science and Technology Project (14CXZ005, AWS15J004, 16BJZ19), National Key R&D Program of China (2019 yearsFF0302300), Construction Project of Key Disciplines in the 13th Five-Year Plan of the PLA (Traumatic Surgery in the Battlefield, 2019-126, 2019-513), Beijing Science and Technology New Star Project (XX2018019/Z181100006218028), the PLA General Hospital Science and technology Project (2019XXJSYX20, 2018XXFC-20, ZH19016)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			

Feng 2021 *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		High risk	

Fiel-Ozores 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) - to identify the main differential clinical features of infection by SARS-CoV-2 **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** every paediatric patient (ages 0-15 years) that had undergone a RT-PCR test for detection of SARS-CoV-2 in a nasopharyngeal sample due to suspected infection was invited for a serology test and interview, setting unclear **Sample size:** n = 126 (33 cases)

Fiel-Ozores 2021 *(Continued)*

	Inclusion criteria: patients aged 0-15 years who underwent RT-PCR test due to clinical suspicion of SARS-CoV-2 during the period under study whose parents/legal guardians provided consent and did not meet any of the exclusion criteria **Exclusion criteria**: patients with serum immunoglobulin (Ig) deficiency. Patients who underwent the RT-PCR test when asymptomatic in the context of contact tracing. Study period: March-May 2020, the months that followed the declaration of the state of alert and the population-wide lock down
Patient characteristics and setting	**Facility cases:** RT-PCR-positive for SARS-CoV-2 **Facility controls**: RT-PCR-negative for SARS-CoV-2 **Country:** Spain **Dates**: March 2020-May 2020 **Symptoms and severity**: not specified, mild to moderate severity **Demographics**: mean age cases 8.4 years, controls 6.5 years M%/F%: cases 66.7/33.3, controls 59.1/40.9 **Exposure history** • cases: 66.7% had close contact with a positive person (pos RT-PCR test), 81.8% had relatives with symptoms • controls: 19.4% had close contact with a positive person (pos RT-PCR test), 9.7% had relatives with symptoms
Index tests	All registered at onset of symptoms and during the course of disease • Fever • Headache • Cough • Asthenia • Diarrhoea • Myalgia • Breathing difficulty • Cutaneous manifestations • Odynophagia • Chills • Wheezing • Anosmia/hyposmia • Rhinorrhoea • Dysgeusia • Abdominal pain • Vomiting
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal swab) + serology: IgA and IgG antibodies 3-4 weeks after the RT-PCR test (blood)
Flow and timing	Timing not specified
Comparative	
Notes	Median time elapsed to the PCR was 8 days and to the first antibody test was 51 days, but interviews were done at time of serology testing (asking about onset of

Fiel-Ozores 2021 *(Continued)*

	symptoms and evolution); unclear which test (PCR or serology) was eventually used as RS Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High

Fiel-Ozores 2021 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Could the patient flow have introduced bias?		High risk

Fink 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) - to define clinical and radiological characteristics of COVID-19 patients within a cohort with respiratory infections in the emergency department **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** patients who presented at the ED of the University Hospital, LMU Munich with signs of a respiratory infection suspicious for COVID-19 **Sample size:** n = 219 (72 cases) **Inclusion criteria**: patients who presented at ED with signs of a respiratory infection suspicious for COVID-19 and received radiological imaging (chest radiographs/chest X-ray and/or CT) as well as RT-PCR for SARS-CoV-2 **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Germany **Dates**: 16 March 2020-12 April 2020 **Symptoms and severity**: mild to moderate to severe. ICU admission: cases 27%, controls 14%. Deaths: cases 5%, controls 3% **Demographics**: age: controls mean 59.5 years, cases mean 60.0 years M%/F%: cases 68.1/31.9, controls 56.5/43.5 **Exposure history**: not specified
Index tests	• Fever (> 38 °C)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection

Fink 2021 *(Continued)*

	• RS: RT-PCR for SARS-CoV-2 (nasopharyngeal and oropharyngeal swab)
Flow and timing	RS and index test both taken at presentation
Comparative	
Notes	Funding: open access funding enabled and organised by Projekt DEAL

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Fink 2021 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Gilbert 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) **Design**: prospective cohort, including consecutive patients with suspected SARS-CoV-2 infection **Recruitment:** all patients presenting to the ED triage centre with symptoms suggestive of COVID-19 **Sample size:** n = 598 (175 cases) **Inclusion criteria**: all consecutive patients suspected of SARS-CoV-2 infection and directed to the triage centres located close to the EDs and subjected to SARS-CoV-2 testing; suspicion = respiratory symptoms and/or fever in a healthcare provider, an immunosuppressed patient or a nursing home resident, and all patients who required admission to the hospital **Exclusion criteria**: none
Patient characteristics and setting	**Facility cases:** RT-PCR-positive patients **Facility controls**: RT-PCR-negative patients **Country:** Belgium **Dates**: 02 March 2020-23 March 2020 **Symptoms and severity**: consecutive patients (selection based on PCR testing), mild to moderate severity (83% sent home for self-isolation, 1.9% ICU, 15% hospital admission) **Demographics**: mean age (all): 41.1 years gender: % female (all): 59.0% **Exposure history**: travel to endemic country: cases 5.1%, controls 12.5% contact with positive patients: cases: 10.9%, controls 9.0%
Index tests	• Flu-like symptoms (myalgia, asthenia, fever) • Mild lower respiratory tract infection symptoms (cough, fever, sputum) • Moderate lower respiratory tract infection symptoms (cough, fever, sputum, dyspnoea) • Upper respiratory tract infection symptoms (sore throat, nasal congestion, sneezing, mild fever) • Respiratory distress signs/symptoms (dyspnoea, cough, fever, low oxygen saturation)

Gilbert 2020 *(Continued)*

	• Isolated fever • Isolated headache • Digestive symptoms (diarrhoea, nausea)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs (> 1 if deemed necessary)
Flow and timing	Index tests followed by reference standard
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Gilbert 2020 *(Continued)*

Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Haehner 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to investigate the frequency of olfactory loss in an outpatient population who presented to a coronavirus testing centre. To evaluate the diagnostic value of the symptom "sudden smell loss" for screening procedures **Design**: cross-sectional cohort study (prospective data collection) **Recruitment:** patients who presented with symptoms of a common cold to a coronavirus testing centre and fulfilled coronavirus testing criteria **Sample size**: n = 500 (cases 34) **Inclusion criteria**: patients with common cold complaints who met the criteria for SARS-CoV-2 testing to WHO recommendations **Exclusion criteria**: none
Patient characteristics and setting	**Facility cases:** RT-PCR for SARS-CoV-2-positive **Facility controls**: RT-PCR for SARS-CoV-2-negative **Country:** Germany **Dates**: not specified **Symptoms and severity**: olfactory loss **Demographics**: mean age: 41.3 years gender % female: 54.6% **Exposure history**: not specified
Index tests	Olfactory loss
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection

Haehner 2020 *(Continued)*

	• RS: RT-PCR, samples from throat swabs
Flow and timing	RS and index test taken on the same day
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			

Haehner 2020 *(Continued)*

Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Haliga 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) - to analyse whether the evaluation of clinical symptoms and signs upon admission to hospital can be useful for the differentiation of patients with acute medical pathology and suspicion of SARS-CoV-2 infection **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** unclear, adult patients presenting to an ED, cohort of patients admitted to our internal medicine clinic at the emergency clinical county hospital; admission through ED, only RT-PCR for patients who were hospitalised **Sample size:** n = 253 (20 cases) **Inclusion criteria**: > 18 years of age, irrespective of gender, admitted to ED due to an acute medical illness as a consequence of exacerbation of their chronic illness as well as symptoms or clinical signs included in the case definition of suspected cases of SARS-CoV-2 infection **Exclusion criteria**: no informed consent, acute pathology requiring specific emergency treatment or PCR already positive at presentation
Patient characteristics and setting	**Facility cases:** RT-PCR-positive for SARS-CoV-2 **Facility controls**: RT-PCR-negative for SARS-CoV-2 **Country:** Romania **Dates**: 01 April 2020- 31 May 2020 **Symptoms and severity**: not specified, mild to moderate to severe: 236 admitted to the clinic and 17 admitted to ICU **Demographics**: mean age overall 64 years M%/F% overall 57.7/42.3 **Exposure history**: not specified
Index tests	• History of fever at home • Fever at presentation • Asthenia • Headache • Dry cough • Sputum production • Chest pain • Dyspnoea

Haliga 2021 *(Continued)*

	• Myalgia • Dysphonia • Sore throat • Anosmia • Dysgeusia • Nausea • Vomiting • Abdominal pain • Diarrhoea • Loss of appetite • Arthralgia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal swab)
Flow and timing	Index tests and RS both taken on admission
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern

Haliga 2021 *(Continued)*

DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Huang 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to explore a novel risk score to predict diagnosis with COVID-19 among all suspected patients at admission **Design**: retrospective, multicentric observational study **Recruitment:** retrospective chart review of patients admitted into 26 COVID-19 designated hospitals in Sichuan Province, China **Sample size:** n = 475 (336 cases) **Inclusion criteria**: patients with suspected COVID-19 (suspected case is defined as having exposure history and 2 clinical manifestations. Patients without epidemiological exposure histories could also be seen as "suspected COVID-19" only if 3 clinical manifestations were present. **Exclusion criteria**: none
Patient characteristics and setting	**Facility cases:** suspected patients with a positive RT-PCR test **Facility controls**: suspected patients with a negative RT-PCR test. If the first test was negative, at least a second test was done, 24 h apart. **Country:** China **Dates**: 21 January 2020-07 February 2020

Huang 2020 *(Continued)*

	Symptoms and severity: mild to moderate severity, all suspected patients included **Demographics**: mean age, cases: 43 years, controls: 34 years. Gender: % female cases 45.8%, controls: 41.0% **Exposure history**: epidemiological exposure history: cases: 69.6%, controls 12.9%
Index tests	• Fever • Headache • Rhinorrhea • Dyspnoea • Wheeze • Dry cough • Haemoptysis • Diarrhoea • Earache • Rash • Enlargement of lymph nodes • Weakness/fatigue • Myalgia • Stuffy nose • Sore throat • Chest pain • Productive cough • Stomach ache • Nausea/vomiting • Arthralgia • Skin ulcer • Unconsciousness
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (if negative, a second test taken at least 24 h apart), sample type not specified
Flow and timing	RS and index tests both taken on admission
Comparative	
Notes	Funding: Emergency Response Project for New Coronavirus of Science and Technology Department of Sichuan Provincial, Grant/Award Numbers: 2020YFS0005, 2020YFS0009; Special Funds for COVID-19 Prevention and Control of West China Hospital of Sichuan University, Grant/Award Number: HX- 2019-nCoV-068; Science and Technology Benefit People Project of Chengdu Municipality, Grant/Award Number: 2016-HM02-00099-SF

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Huang 2020 *(Continued)*

Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Hüfner 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) - to identify patients in the ED early using a score so that they can be isolated pre-emptively **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all patients who presented at 1 of 3 ED's **Sample size:** n = 697 (64 cases) **Inclusion criteria**: all patients presenting at one of the participating EDs and scoring at least 1 item of the COVID score **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Germany **Dates**: 9 March 2020-30 April 2020 **Symptoms and severity**: all symptomatic patients, 79.7% of cases hospitalised, 53.1% of controls **Demographics**: age: controls mean 54.7 years, cases mean 60.3 years M%/F%: cases 68.8/31.2, controls 46.9/53.1 **Exposure history**: not specified
Index tests	• Fever > 37.3 ° C and/or chills • (Irritant) cough with/without sputum • Impairment of the sense of smell or taste • Sore throat • Fatigue (malaise, tiredness) • Headache • Body aches (muscles, joints) • Runny nose • GI symptoms (unspecific abdominal complaints, diarrhoea, vomiting)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (nasopharyngeal and oropharyngeal swab) or chest X-ray or CT
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared
Methodological quality	

Hüfner 2020 *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Unclear
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
Could the patient flow have introduced bias?		Unclear risk	

Ide 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) - to evaluate the SARS-CoV-2-positive ratio among mildly ill patients in Tokyo, Japan, their characteristics, the Ministry of Health, Labour and Welfare criteria, and to identify better criteria **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** patients who underwent SARS-CoV-2 PCR testing at the National Center for Global Health and Medicine in Tokyo (= outpatient screening centre) **Sample size:** n = 277 (25 cases) **Inclusion criteria**: those who met ≥ 1 of the following criteria were eligible: patients who have fever or symptoms (e.g. respiratory, fatigue, headache, myalgia); patients who had exposure to COVID-19 patient; patients who did not meet 1) or 2) but referred by another physician due to possible exposure to COVID-19 patient or travel history. **Exclusion criteria**: patients who were non-ambulatory upon presentation (referred to the infectious disease clinic for further evaluation)
Patient characteristics and setting	**Facility cases:** RT-PCR-positive for SARS-COV-2 **Facility controls**: RT-PCR-negative for SARS-COV-2 **Country:** Japan **Dates**: 09 March 2020-29 March 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: age: controls median 38.9 years, cases median 44.1 years M%/F%: cases 88.0/12.0, controls 52.0/48.0 **Exposure history**: exposure to case: cases 52%, controls 7%; travel: cases 72%, controls 20%
Index tests	• Fever (> 37.5 °C) • Nasal discharge • Sore throat • Cough • Sputum • Dyspnoea • Fatigue • Headache • Myalgia/joint pain • Diarrhoea • Vomiting
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs
Flow and timing	Timing not specified

Ide 2021 *(Continued)*

Comparative	
Notes	Funding: grant for International Health Research from the Ministry of Health Labor and Welfare of Japan (grant no. 20A2003D)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			

Ide 2021 *(Continued)*

Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Ishii 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to identify the predictors of SARS-CoV-2 test positivity for more efficient and evidenced selection of suspected individuals **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all consecutive individuals, tested in a drive-through outpatient test centre during the first 7 months of the testing programme **Sample size:** n = 3540 (164 cases) **Inclusion criteria**: all consecutive participants who underwent drive-through nasopharyngeal swab testing at an outpatient clinic. Reason for testing: upon request of the participant or participants who had been confirmed to have contacted COVID-19 patients based on contact tracing. No clinical suspicion needed per se, but 54% of individuals were symptomatic, suggestive of COVID-19 **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Japan **Dates**: 16 July 2020-31 January 2021 **Symptoms and severity**: not specified, 54% of individuals presented with symptoms suggestive of COVID-19, mostly mild severity **Demographics**: age: controls median 27 years, cases median 25 years M%/F%: cases 63.4/36.6, controls 49.4/50.6 **Exposure history**: history of close contact with COVID-19 patient: cases 44%, controls 26%
Index tests	• Body temperature (fever defined as ≥ 38.0 °C) • Cough • Dyspnoea
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swab

Ishii 2021 *(Continued)*

Flow and timing	Timing not specified
Comparative	
Notes	No clinical suspicion needed for testing Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Ishii 2021 *(Continued)*

DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

Jeyashree 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the symptom profile of people who underwent testing for COVID-19 **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all consecutive adults who visited COVID-19 testing centres in Chennai city in Southern India **Sample size:** n = 277 (58 cases) **Inclusion criteria**: all consenting adults aged 18-80 years belonging to any gender, who visited COVID-19 testing centres in Chennai city in Southern India **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** India **Dates**: not specified (2020) **Symptoms and severity**: not specified, mild to moderate severity **Demographics**: overall age: mean 40.7 years M%/F%: cases 51.7/48.3, controls 63.5/36.5 **Exposure history**: history of close contact with COVID-19 patient: cases 9%, controls 5%
Index tests	• Fever • Headache • Cough • Runny nose • Joint pain • Muscle aches • Sore throat • Fatigue/malaise • Loss of smell or taste

Jeyashree 2021 *(Continued)*

	• Loss of smell • Loss of appetite • Chills • Loss of taste • Vomiting • Altered conscious • Bleeding • DIarrhoea • Conjunctivitis • Wheezing • Chest pain • Skin rash • Pain abdomen • Shortness of breath
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swab
Flow and timing	Index tests were collected on same day of the specimen collection, and prior to the declaration of COVID-19 test results
Comparative	
Notes	Funding: supported by the Indian Council of Medical Research- National Institute of Epidemiology (ICMR-NIE)

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	

Jeyashree 2021 *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Just 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to identify predictive risk factors for a positive SARS-CoV-2 RT-PCR result in a primary care setting **Design**: multicentre, cross-sectional cohort study **Recruitment:** 26 office-based specialists for internal and/or general medicine with a full primary care mandate from 14 different locations participated in the study. Suspected COVID-19 patients for whom a PCR was taken were included. **Sample size:** n = 374 (40 cases) **Inclusion criteria**: convenience sample of patients who received PCR in the participating GPs' practices within the study period **Exclusion criteria**: patients whose tests had been carried out for procedural reasons and did not correspond to a specific clinical indication were excluded (e.g. testing of recovered patients after end of quarantine). There were no other exclusion criteria.
Patient characteristics and setting	**Facility cases:** suspected patients with a positive PCR test **Facility controls**: suspected patients with a negative PCR test **Country:** Germany

Just 2020 *(Continued)*

	Dates: 24 March 2020-17 April 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: median age: cases: 52.0 years, controls: 43.5 years gender: % female cases: 65.0%, controls: 57.2% **Exposure history**: first grade contact (with symptoms): cases: 35.0%, controls 17.4%
Index tests	• Cough • Sore throat • Fatigue • Fever • Nasal congestion • Muscle pain • Dyspnoea • Headache • Anorexia • Anosmia • Diarrhoea • Chills • Nausea • Vomiting • Other
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, sample type not specified
Flow and timing	RS and index tests both taken on admission
Comparative	
Notes	Funding: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern

Just 2020 *(Continued)*

DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Kalayjian 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to assess the rate of COVID-19 positivity in a community-based health centre, evaluate the clinical symptoms, and follow patient outcomes **Design**: cross-sectional cohort study, prospective data collection **Recruitment**: clients entering the health centre (walk-in clinic) were screened for symptoms and triaged to the COVID-19 clinic. Testing was performed for patients with a documented or subjective fever within the past 72 h. **Sample size:** n = 345 (117 cases)

Kalayjian 2020 *(Continued)*

	Inclusion criteria: people ≥ 17 years old, screened for COVID-19 symptoms and triaged, a documented or subjective fever within the past 72 h **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** patients with a positive Labcorp's nucleic-acid amplification nasopharyngeal swab for SARS-CoV-2 **Facility controls**: patients with a negative Labcorp's nucleic-acid amplification nasopharyngeal swab for SARS-CoV-2 **Country:** Louisiana, USA **Dates**: 16 March 2020-10 April 2020 **Symptoms and severity**: walk-in clinic for people with COVID-19 symptoms; 9 required ED assessment of whom 6 were admitted to hospital; all patients had to have fever in the past 72 h **Demographics**: age: controls mean 44.4 years, cases mean 42.3 years M%/F%: cases 49.6/50.4, controls 46.5/50.4 (3.1% "other") **Exposure history**: not specified
Index tests	• Body temperature • Heart rate • Oxygen saturation • Cough • Shortness of breath • Sore throat • Nasal congestion • GI symptoms
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: Labcorp's nucleic-acid amplification, threshold not specified, nasopharyngeal swabs
Flow and timing	Index tests and reference standard taken at the same clinical encounter
Comparative	
Notes	Only feverish patients included Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		

Kalayjian 2020 *(Continued)*

Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Low risk	

Kelen 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to understand the impact of COVID-19 on EDs **Design**: cross-sectional cohort study, retrospective data collection

Kelen 2021 *(Continued)*

	Recruitment: consecutive: all patients of at least 15 years of age presenting at ED with symptoms suggestive of COVID-19 or with high acuity **Sample size:** n = 11402 (2484 cases) **Inclusion criteria**: at least 15 years old and symptoms suggestive of COVID-19 symptoms or high acuity **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** USA **Dates**: 16 March 2020-15 May 2020 **Symptoms and severity**: mild to moderate severity; acuity triage score 1 (highest) 4.7%; 2 22.9%; 3 55.3%; 4 14.1%; 5 1.6%; not listed 1.3% **Demographics**: age overall: 15-24 years: 31.8%, 25-34 years: 33.7%, 35-44 years: 39.3%, 45-54 years: 42.1%, 55-64 years: 45.2%, 65-74 years: 48.1%, 75+ years: 52.6% M%/F%:overall (all those tested) 40.7/59.3 **Exposure history**: not specified
Index tests	• Fever • Constitutional symptom • Pulmonary • Hypotension • Shortness of breath • Altered mental status • Weakness • Syncope • Headache • Nausea/vomiting/diarrhoea • Obstetric/gynaecological symptoms (pregnancy related)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs
Flow and timing	Index test and RS both taken upon arrival at ED
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Kelen 2021 *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Kempker 2020

Study characteristics			

Kempker 2020 *(Continued)*

Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the most common and distinguishing clinical symptoms among HCWs who underwent screening for COVID-19 **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** HCW with a viral-like illness, triaged to the employee health services staff for a virtual clinical assessment and then scheduled for SARS-CoV-2 testing **Sample size:** n = 283 (51 cases) **Inclusion criteria**: HCW with symptoms consistent with a viral-like illness **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** HCW with positive RT-PCR test for SARS-CoV-2 **Facility controls**: HCW with negative RT-PCR test for SARS-CoV-2 **Country:** Georgia, USA **Dates**: 18 March 2020-14 April 2020 **Symptoms and severity**: not specified, mild to moderate severity (from table) **Demographics**: age: not specified M%/F%: overall 19/81 **Exposure history**: patient contact in general: cases: 96%, controls 88%. Contact with COVID-19 patients: cases 33%, control 36%
Index tests	• Fever • Fatigue • Chills • Myalgia • Cough • Dyspnoea • Nasal congestion • Sore throat • Diarrhoea • Anosmia • Ageusia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swab
Flow and timing	Not specified
Comparative	
Notes	Funding: none declared
Methodological quality	

Kempker 2020 *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Kim 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to develop a prediction rule for COVID-19 **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** consecutive: all patients > 18 years visiting ED who had undergone COVID-19 testing **Sample size:** n = 242 (54 cases) **Inclusion criteria**: > 18 years and visit to one of the EDs **Exclusion criteria**: - if initial signs and symptoms were not recorded - in the case of a revisit
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** South Korea **Dates**: 1 March 2020-21 March 2020 **Symptoms and severity**: mild to moderate to severe: admission to ward: cases 48.1% controls 0% Admission to ICU cases 11.5% controls 0%, in-hospital death cases 20.4% controls 0% **Demographics**: age: controls median 43.5 years, cases median 70.0 years M%/F%: cases 55.6/44.4, controls 45.2/54.8 **Exposure history**: any exposure risk: 37.2% overall
Index tests	• Systolic BP • Diastolic BP • Pulse rate • Respiratory rate • Body temperature • Oxygen saturation • Mild fever ≥ 37.5 • Tachypnoea • Oxygen saturation ≤ 94% • Fever • Cough or dyspnoea • Sore throat
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs
Flow and timing	Index test and RS both taken upon arrival at ED
Comparative	

Kim 2020 *(Continued)*

Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		

Kim 2020 *(Continued)*

Could the patient flow have introduced bias?	Low risk

King 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to assess symptom patterns among children tested for SARS-CoV-2 **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** database study (Alberta Health Services Communicable Disease Outbreak Management database), including data on children with a positive test result or children tested for contact with a case or in an outbreak **Sample size:** n = 3249 (2264 cases), after exclusions: n = 2463 (1978 cases) **Inclusion criteria**: patients < 18 years with a positive PCR test or were tested for being in a high-risk group (close contact with a case or in an outbreak) **Exclusion criteria**: second tests or patients tested prior to 13 April 2020. Children who were tested for symptoms and were negative, were not contacted for the symptom questionnaire.
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Canada **Dates**: 13 April 2020-30 September 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: age: controls mean 8.4 years, cases mean 9.8 years; M%/F %: cases 49.4/50.6, controls 53.6/46.4 **Exposure history**: not specified
Index tests	• Anosmia/ageusia • Nausea/vomiting • Headache • Decreased appetite/anorexia • Sneezing • Fever or feverish chills • Muscle/joint pain • Malaise • Nasal congestion • Fatigue • Difficulty breathing/dyspnoea • Sore throat • Diarrhoea • Cough • Rhinorrhoea • Chest pain

King 2020 *(Continued)*

	• Conjunctivitis
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasal, nasopharyngeal, throat, or other swabs
Flow and timing	Maximum 5 days between index tests and RS (RS came first in some cases)
Comparative	
Notes	Funding: FM was funded by an Alberta Health Services Chair in Cardiovascular Outcomes Research; project was funded by the Alberta Strategy for Patient Oriented Research Support Unit

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	No		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

King 2020 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	No		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		High risk	

Krastinova 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe infection rates, clinical characteristics, occupational exposure, living conditions and household transmission of symptomatic HCWs **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** symptomatic HCWs in 1 hospital were tested on a voluntary basis (ED/outpatient setting) **Sample size:** n = 314 (110 cases) **Inclusion criteria**: symptomatic HCWs, defined as the presence of fever and/or respiratory symptoms **Exclusion criteria**: none specified
Patient characteristics and setting	**Definition cases:** positive RT-PCR test for SARS-CoV-2 **Definition controls**: negative RT-PCR test for SARS-CoV-2 **Country:** France **Dates**: 17 March 2020-20 April 2020 **Symptoms and severity**: mild to moderate severity, 0% of controls hospitalised, 8% of cases hospitalised **Demographics**: age: controls mean 40.2 years, cases mean 40.3 years M%/F%: cases 20.0/80.0, controls 18.0/82.0 **Exposure history**: not specified
Index tests	At illness onset: • fever • cough • dyspnoea • tiredness

Krastinova 2020 *(Continued)*

- sore throat
- rhinorrhoea/nasal congestion
- headache
- muscle pain
- chest pain/pressure
- nausea, vomiting
- diarrhoea
- anosmia

At screening:

- heart rate
- oxygen saturation
- fever
- cough
- dyspnoea
- tiredness
- sore throat
- rhinorrhoea/nasal congestion
- headache
- muscle pain
- chest pain and/or pressure
- nausea and/or vomiting
- diarrhoea
- anosmia

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern

Krastinova 2020 *(Continued)*

DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Langer 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to develop a model to predict the results of RT-PCR **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all patients admitted to ED with symptoms compatible with COVID-19 **Sample size:** n = 199 (124 cases) **Inclusion criteria**: all patients presenting with symptoms compatible with COVID-19 **Exclusion criteria**: < 12 years, no leukocyte formula

Langer 2020 *(Continued)*

Patient characteristics and setting	**Definition cases:** positive RT-PCR test for SARS-CoV-2 **Definition controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Italy **Dates**: 22 February 2020-16 March 2020 **Symptoms and severity**: inclusion based on potential COVID-19 symptoms, mostly mild to moderate symptoms, oxygen supplementation needed in 22% of cases and 32% of controls **Demographics**: age: controls median 66 years, cases median 65 years M%/F%: cases 62.9/37.1, controls 65.3/34.7 **Exposure history**: not specified
Index tests	• Arthralgia • Asthenia • Chest pain • Cough • Dyspnoea • Fever • GI symptoms • Headache • Sore throat • Syncope • Glasgow coma scale • Body temperature • Systolic BP • Diastolic BP • Heart rate • Sinus rhythm • Respiratory rate
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, specimen not specified, repeated after 48 h if negative
Flow and timing	Index tests and RS both on admission, but in case of a negative PCR the test was repeated after 48 h
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		

Langer 2020 *(Continued)*

Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Lazzerini 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe characteristics and risk factors for COVID-19 in children

Lazzerini 2021 *(Continued)*

	Design: cross-sectional cohort study, retrospective data collection **Recruitment**: all children aged 0-18 years tested for SARS-CoV-2 at 1 of 20 paediatric centres across Italy because of symptoms/signs suggestive of COVID-19 **Sample size:** n = 2148 (159 cases) **Inclusion criteria**: children (0-18 years) tested because of symptoms suggestive of COVID-19 **Exclusion criteria**: none
Patient characteristics and setting	**Definition cases:** positive RT-PCR test for SARS-CoV-2 **Definition controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Italy **Dates**: 23 February 2020-24 May 2020 **Symptoms and severity**: inclusion based on potential COVID-symptoms, mostly mild to moderate symptoms, among the cases, only 2.1% required respiratory support and 1.1% were admitted to intensive care; all recovered **Demographics**: age: < 6 months: cases 12%, controls 8%; 6-24 months: cases 10.7%, controls 23.7%; 2-9 years: cases 23.3%, controls 42%; 10-18 years: cases 54.1%, controls 26% M%/F%: cases 48.4/51.6, controls 55.8/44.2 **Exposure history**: contact with person having COVID-19: cases 79.2%, controls 6.1%; relatives with respiratory symptoms: cases 72.3%, controls 11.5%

Index tests	• Symptoms and signs at presentation:
	  ◦ fever
	  ◦ respiratory symptoms, any
	  ◦ respiratory distress
	  ◦ rhinorrhoea
	  ◦ dry cough
	  ◦ productive cough
	  ◦ sore throat
	  ◦ pharyngitis
	  ◦ conjunctivitis
	  ◦ apnoea
	  ◦ thoracic pain
	• GI symptoms, any:
	  ◦ vomiting
	  ◦ diarrhoea
	• Neurological symptoms, any:
	  ◦ asthenia
	  ◦ headache
	  ◦ anosmia/ageusia
	  ◦ convulsion
	  ◦ hyperactivity
	• Cutaneous presentations, any:
	  ◦ skin manifestation
	  ◦ vasculitis

Lazzerini 2021 *(Continued)*

	• Unspecific influenza-like presentations, any:
	  ○ muscle or joint pains
	  ○ nausea
	  ○ inappetence
	  ○ lymphadenitis
	• Other symptoms, any:
	  ○ abdominal pain
	  ○ oral manifestations (gingivostomatitis, aphthae)
	  ○ dental problems
	  ○ urogenital disorder
	  ○ ear problems
	  ○ other
	• Tachycardia
	• Tachypnoea
	• Oxygen saturation
	• Lung auscultation findings

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasal or nasopharyngeal swab
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		

Lazzerini 2021 *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Leal 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the clinical features predictive for SARS-CoV-2 infection in primary care **Design**: prospective population-based cohort **Recruitment:** residents of the municipality aged ≥ 12 years with suspected COVID-19 symptoms were encouraged to contact the dedicated platform via the website or phone. They were invited to complete an initial screening questionnaire. Participents were then called by a medical student to complete a risk assessment. **Sample size:** n = 1583 (444 cases (only the PCR-positive patients) **Inclusion criteria**: patients meeting the suspected COVID-19 case definition (having at least 2 of the following symptoms: fever, cough, sore throat, coryza or change in/loss of smell (anosmia); or 1 of these symptoms plus at least 2 other symptoms consistent with COVID-19

Leal 2020 *(Continued)*

	Exclusion criteria: all pregnant women, and patients meeting pre-defined triage criteria for severe disease
Patient characteristics and setting	**Facility cases:** patients with suspected COVID-19 who tested positive (RT-PCR, testing at home) **Facility controls**: patients with suspected COVID-19 who tested negative (RT-PCR, testing at home) **Country:** Brazil **Dates**: 13 April 2020-13 May 2020 **Symptoms and severity**: mild to moderate severity, severe cases were excluded **Demographics**: all age groups represented from ≥ 10 years. Gender: % female cases: 55.0%, controls: 66.5% **Exposure history**: not specified
Index tests	• Headache • Myalgia • Cough • Fatigue • Anosmia • Ageusia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, some negative patients were offered antibody testing as of 19 May 2020 (IgG/IgM combined); self-collected oropharyngeal swabs, collected under supervision of trained HCWs), but results of the antibody testing were not used for this review (only RT-PCR)
Flow and timing	Swabs were taken within 5 days of symptom onset
Comparative	
Notes	Funding: the municipal health department of São Caetano do Sul funded the establishment and implementation of the platform. Plus award from FAPESP (2018/14389-0) and the UK Medical Research Council (MR/S0195/1) to the Brazil-UK Centre for Arbovirus Discovery

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		

Leal 2020 *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		High risk	

Leung 2021

Study characteristics	

Leung 2021 *(Continued)*

Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to review the characteristics and outcomes of individuals who attended a testing centre **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all patients attending the testing centre (temporary outpatient testing centre at the AsiaWorldExpo) **Sample size:** n = 1258 (86 cases) **Inclusion criteria**: all patients presenting to the testing centre **Exclusion criteria**: missing data and immediate referral to regional ED
Patient characteristics and setting	**Definition cases:** positive RT-PCR test for SARS-CoV-2 **Definition controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Hong Kong (China) **Dates**: 20 March 2020-19 April 2020 **Symptoms and severity**: 96% of all participants symptomatic, mostly mild severity, acutely ill patients were immediately referred to ED **Demographics**: age: controls mean 27.1 years, cases mean 30.6 years M%/F%: cases 53.5/46.5, controls 51.7/48.3 Non-Chinese ethnicity overall 10% **Exposure history**: not specified
Index tests	• Fever • Documented fever • Reported fever • Chills • Cough • Runny nose • Sore throat • Vomiting • Diarrhoea • Fatigue • Myalgia • Headache • Anosmia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, pooled nasopharyngeal and throat swabs
Flow and timing	Timing not specified, but both index tests and RS taken at outpatient test centre, so all tests and assessments should have been done at the time of presentation
Comparative	
Notes	Funding: none declared

Leung 2021 *(Continued)*

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Low risk	

Maechler 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe epidemiological and clinical characteristics; to identify risk factors for SARS-CoV-2 infection **Design**: cross-sectional cohort study, prospective data collection **Recruitment**: symptomatic patients presenting at the test site. Subgroups not by testing criteria at that time: (1) high-risk contacts at a nightclub (26/94 positive). (2) Charité employees 125 asymptomatic. **Sample size:** n = 4333 (333 cases) **Inclusion criteria**: until 24 March 2020: symptomatic patients with high-risk contacts or return from high-risk area. From 24 March: also symptomatic people with risk factors and if the test capacity allowed also only symptomatic patients. Plus 2 subgroups of high-risk patients in a nightclub and Charité employees **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** patients with a positive RT-PCR for SARS-CoV-2 infection **Facility controls**: patients with a negative RT-PCR for SARS-CoV-2 infection **Country:** Germany **Dates**: 03 March 2020-13 April 2020 **Symptoms and severity**: mild to relatively more severe. Asymptomatic: 12 cases, 431 controls **Demographics**: age: controls median 34.0 years, cases mean 34.0 years M%/F%: cases 56.8/43.2, controls 48.5/51.5 **Exposure history**: high-risk contact: cases 56.8%, controls 36.4%
Index tests	• Fever • Dyspnoea • Chest tightness/pain • Chills • Fatigue • Body aches • Cough • Rhinorrhoea • Diarrhoea • Sore throat • Headache • Anosmia • Ageusia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (combined oro- and nasopharyngeal swab)

Maechler 2020 *(Continued)*

Flow and timing	Index tests and reference standard both at presentation		
Comparative			
Notes	Funding: none declared		

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			

Maechler 2020 *(Continued)*

Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Mansella 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to evaluate safety and feasibility of low-threshold testing process; to identify clinical predictors for severe acute COVID-19 **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all patients presenting at the test centre with respiratory symptoms (such as shortness of breath), other flu-like symptoms (fever, sore throat, cough) and self-reported exposure to COVID-19 **Sample size:** n = 4815 (572 cases) **Inclusion criteria**: all patients presenting at the test centre with respiratory symptoms, flu-like symptoms and self-reported exposure to COVID-19 **Exclusion criteria**: no informed consent, no nasopharyngeal swab and missing data
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Switzerland **Dates**: 19 March 2020-19 April 2021 **Symptoms and severity**: mostly mild to moderate severity, 41/4815 (0.9%) participants were hospitalised **Demographics**: age: controls median 41.2 years, cases median 45.7 years M%/F%: cases 50.5/49.5, controls 44.8/55.2 **Exposure history**: not specified
Index tests	• Measured/reported • Fever • Chills • Myalgia • Lymphadenopathy • Headache • Seizure • Confusion • Nausea • Conjunctivitis

Mansella 2020 *(Continued)*

	• Exanthema • Coryza • Otalgia • Sore throat • Dyspnoea • Wheezing • Cough • Productive cough • Haemoptysis • Chest pain • Abdominal pain • Diarrhoea • Dysuria • Exhausted • Weakness
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, 2 swabs from naso- and oropharyngeal sites combined into 1
Flow and timing	Index tests and RS probably both at presentation, but not specified
Comparative	
Notes	Funding: supported by Scientific funds from the University Hospital Basel Switzerland

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		

Mansella 2020 *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Low risk	

Mao 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to ascertain the effectiveness of the screening strategy and provide insight for early diagnosis of COVID-19 **Design**: multicenter, retrospective, observational cohort study **Recruitment:** all patients visiting the fever clinics within the study period **Sample size**: n = 1004 (cases = 188) **Inclusion criteria**: all patients visiting the fever clinics within the study period. Patients with fever (body temperature > 37.5 °C), or patients with pulmonary symptoms and epidemiological exposure history were requested to visit the fever clinics. All patients visiting the fever clinics during the study period were included. **Exclusion criteria**: patients with missing data
Patient characteristics and setting	**Facility cases:** RT-PCR-positive patients

Mao 2020 *(Continued)*

	Facility controls: RT-PCR-negative patients **Country:** China **Dates**: 17 January 2020-16 February 2020 **Symptoms and severity**: not specified **Demographics**: median age: cases 46 years, controls 39 years. Female; gender %: cases 50%, controls 47% **Exposure history**: recent visit to epidemic region: cases 51%, controls 28%; contact with infected person: cases 34%, controls 13%
Index tests	• Fever (body temperature > 38.5 °C) • Chills • Cough • Sore throat • Nasal congestion • Rhinorrhea • Sneezing • Shortness of breath • Haemotysis • Chest pain • Fatigue • Headache • Abdominal pain • Diarrhoea • Nausea/vomiting • Poor appetite • Myalgia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (specimen not specified)
Flow and timing	RS and index tests taken on the same day
Comparative	
Notes	Funding: National Natural Science Foundation of China

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Unclear		

Mao 2020 *(Continued)*

Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Martín-Sánchez 2020

Study characteristics	
Patient Sampling	**Purpose**: diagnosis of SARS-CoV-2 infection (mild to severe COVID-19 disease); to describe the clinical characteristics and 30-day mortality rates in ED patients with COVID-19 in different diagnostic groupings **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** COVID-19 suspects treated in the emergency room

Martín-Sánchez 2020 *(Continued)*

	Sample size: n = 1417 (1190 cases) (after exclusion of all participants without an RT-PCR) **Inclusion criteria**: all suspicious cases of COVID-19 served in the ED of the San Carlos Clinical Hospital **Exclusion criteria**: patients with a positive PCR test prior to assessment in the ED
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Spain **Dates**: 28 February 2020-31 March 2020 **Symptoms and severity**: 30-day mortality was 11.5% (56.5% in hospitalised cases and 19.6% in cases classified as severe) **Demographics**: age: controls median 50.7 years, cases median 61.5 years M%/F%: cases 53.5/46.5, controls 37.4/62.6 **Exposure history**: not specified
Index tests	• Cough • Dystermic sensation • Dyspnoea • Thoracic pain • Diarrhoea • Nausea/vomiting • Headache • Confusion • Anosmia • Dysgeusia • Myalgia • Asthenia • Odynofagia • Nasal congestion • Cutaneous lesions • Syncopes • Body temperature • Pulse • Oxygen saturation • BP
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasal- and oropharyngeal swabs)
Flow and timing	Index tests and reference standard both taken at the ED
Comparative	
Notes	Strong preselection of participants, unclear why some were not tested, very high disease prevalence

Martín-Sánchez 2020 *(Continued)*

Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		

Martín-Sánchez 2020 *(Continued)*

Could the patient flow have introduced bias?	Low risk

Martin-Sanz 2020

Study characteristics	
Patient Sampling	**Purpose**: diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to evaluate the incidence of certain symptoms in a population of HCWs (exposed to COVID-19-positive patients) **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** HCW of the University Hospital of Getafe (Madrid, Spain) with suspicion of COVID-19 infection **Sample size:** n = 355 (215 cases) **Inclusion criteria**: HCW with suspicion of COVID-19 infection. Suspicion of COVID-19 was determined by the presence of either cough, fever (> 37.5 °C), headache, or breathlessness, regardless of contact with a COVID-19 patient **Exclusion criteria**: inconclusive PCR results
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Spain **Dates**: 15 March 2020-07 April 2020 **Symptoms and severity**: mild to moderate severity (only 14 patients (3.94%) developed pneumonia or severe symptoms that required hospitalisation) **Demographics**: age: overall mean 42.9 years (SD = 0.67) M%/F%: cases 20.5/79.5, controls 17.1/82.9 **Exposure history**: not specified
Index tests	• Cough + hyposmia • Hyposmia • Dysthermia + hyposmia • Hypogeusia • Dysthermia • Cough • Myalgia • Asthenia • Rhinorrhea • Back pain • Chest pain • Dyspnoea • Diarrhoea • Headache • Sore throat

Martin-Sanz 2020 *(Continued)*

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 next-generation sequencing or real-time PCR methods (nasal and pharyngeal swabs)
Flow and timing	Not specified
Comparative	
Notes	Article states that it is a case-control study, while it is not (all consecutive suspected HCW's enrolled and tested) Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Martin-Sanz 2020 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Unclear	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Nazerian 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to formally evaluate the diagnostic testing characteristics of physicians' gestalt for COVID-19 **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** patients with suspected COVID-19 were prospectively enrolled in 2 EDs **Sample size:** n = 838 (193 cases) **Inclusion criteria**: age ≥ 18 years, presence of any sign or symptom for COVID-19 and first evaluation at ED during the study period **Exclusion criteria**: known diagnosis of COVID-19, loss to follow-up and refusal to participate
Patient characteristics and setting	**Definition cases:** positive RT-PCR test for SARS-CoV-2 or suggestive symptoms plus chest imaging of acute interstitial lung disease in the absence of an alternative diagnosis taking into account all 30-day follow-up data including medical data and a structured telephone interview **Definition controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Italy **Dates**: 01 April 2020-30 April 2020 **Symptoms and severity**: mostly mild to moderate severity, need of oxygen supplementation or ventilation: cases 37%, controls 25% **Demographics**: age: controls median 70 years, cases mean 69 years M%/F%: cases 52.3/47.7, controls 49.5/50.5 **Exposure history**: not specified
Index tests	• Fever • Cough • Pharyngodynia

Nazerian 2021 *(Continued)*

	• Dyspnoea • Anosmia • Ageusia • Fatigue • Diarrhoea • Symptom duration
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, positive result within 5 days after ED presentation, *or* suggestive symptoms plus chest imaging (showing acute interstitial lung disease in the absence of an alternative diagnosis), *or* panel adjudication (for 3 cases without a positive PCR); any respiratory specimen
Flow and timing	Max 5 days for PCR test, up to 30 days for clinical information
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			

Nazerian 2021 *(Continued)*

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Low risk	

Nitecki 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to assess the utility of self-reported symptoms in identifying positive COVID-19 cases among predominantly healthy young adults in a military setting **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all individuals who were deemed eligible for COVID-19 testing by the Israel Defence Forces COVID Centre, including those voluntarily calling to report symptoms, those actively addressed following epidemiological investigation **Sample size:** n = 24362 (1338 cases) **Inclusion criteria**: all individuals who were deemed eligible for COVID-19 testing by the Israel Defence Forces COVID Centre (suspicious symptoms, those quarantined), including those voluntarily calling to report symptoms, those actively addressed following epidemiological investigation **Exclusion criteria**: no informed consent, no nasopharyngeal swab and missing data
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Israel **Dates**: 26 March 2020-02 August 2020

Nitecki 2021 *(Continued)*

	Symptoms and severity: mostly mild to moderate severity, mostly cough (56.1%) and fever (28.3%) **Demographics**: age: controls median 21 years, cases median 21 years M%/F%: cases 61.1/38.9, controls 59.0/41.0 **Exposure history**: suspected exposure 50.1% (defined as close contact with a confirmed COVID-19 patient or recent (< 14 days) international travel)
Index tests	• Cough • Fever • Sore throat • Rhinorrhoea • Loss of taste or smell • Chest pain • GI symptoms
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		

Nitecki 2021 *(Continued)*

Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Unclear risk	

O'Reilly 2020a

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to determine the clinical and epidemiological predictors of a positive SARS-CoV-2 test result and the requirement for intensive respiratory support **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** adult patients who meet testing criteria for COVID-19 and have a SARS-CoV-2 PCR test requested in the ED **Sample size:** n = 240 (cases = 11) **Inclusion criteria**: all adults who met the testing criteria for COVID-19 and who presented at the ED **Exclusion criteria**: patients who attended the screening clinic and did not present for medical assessment in the ED (no clinical data available)
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2

O'Reilly 2020a *(Continued)*

	Facility controls: negative RT-PCR for SARS-CoV-2 **Country:** Australia **Dates**: 01 April 2020-14 April 2020 **Symptoms and severity**: moderate to severe **Demographics**: mean age: cases 51 years, controls 61 years M%/F%: cases 72.0/28.0, controls 55.0/45.0 **Exposure history**: contact with infected person: cases 56%, controls 7%
Index tests	• Shortness of breath • Cough • Change to chronic cough • Anosmia/dysgeusia • Sore throat • Runny nose • Fever • Fatigue • Myalgia • Diarrhoea
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (specimen not specified)
Flow and timing	RS and index tests taken on the same day
Comparative	
Notes	Funding: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			

O'Reilly 2020a *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

O'Reilly 2020b

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the epidemiology and clinical features of patients presenting to the ED with suspected and confirmed COVID-19 **Design**: cross-sectional cohort study, prospective data collection **Recruitment**: all adult patients who met criteria for "suspected COVID-19" and underwent testing for SARS-CoV-2 were eligible for inclusion. "Testing criteria are guided by the various health jurisdictions and have evolved throughout the project." **Sample size:** n = 1334 (50 cases) **Inclusion criteria**: adult patients who had a SARS-CoV-2 PCR test requested in the ED and were managed as "suspected COVID-19"

O'Reilly 2020b *(Continued)*

	Exclusion criteria: patients who underwent testing for surveillance purposes
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Australia **Dates**: 01 July 2020-31 July 2020 **Symptoms and severity**: all levels of severity, mostly mild to moderate **Demographics**: mean age: cases 53 years, controls 56 years M%/F%: cases 48.0/52.0, controls 50.0/50.0 **Exposure history**: 50% reported close contact with a confirmed case of COVID-19 or a positive SARS-CoV-2 PCR swab result in the 14 days prior to their ED presentation
Index tests	• Shortness of breath • Cough • Anosmia or dysgeusia • Sore throat • Runny nose • Fever • Fatigue • Myalgia • Diarrhoea • Body temperature • Fever recorded • Oxygen saturation (SaO2) • Hypoxia (cut-off SaO2 < 92%) • Systolic BP • Diastolic BP • Hypotension • Abnormality on chest auscultation
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasopharyngeal swab)
Flow and timing	Index tests and reference standard both taken at presentation in the ED
Comparative	
Notes	Thresholds only specified for vital parameters, not for most symptoms Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

O'Reilly 2020b *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Unclear risk	

Olivar Lopez 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the profile of patients < 18 years of age treated at a paediatric COVID centre and its association with test confirmation, endotracheal intubation and death **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all patients < 18 years who presented with a clinical picture compatible with COVID-19 (= fever, respiratory symptoms or general malaise) at the ED of a COVID paediatric reference hospital **Sample size:** n = 510 (79 cases) **Inclusion criteria**: all patients < 18 years with symptoms compatible with COVID-19 (= fever, respiratory symptoms or general malaise), and who underwent PCR testing **Exclusion criteria**: unreported test results, insufficient or poorly taken samples
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Mexico **Dates**: March 2020-June 2020 **Symptoms and severity**: mild to moderate to severe, 12.3% of controls and 19.3% of cases intubated **Demographics**: age: controls mean 5 years, cases mean 4.9 years M%/F%: cases 59.5/40.5, controls 51.7/48.3 **Exposure history**: contact with case: 57.9% of cases, 27.6% of controls
Index tests	• Fever • Cough • Odynophagia • Dyspnoea • Irritability • Diarrhoea • Chest pain • Shivers • Headache • Myalgia • Arthralgia • General malaise • Rhinorrhoea • Polypnoea • Vomiting • Abdominal pain • Conjunctivitis • Cyanosis

Olivar Lopez 2020 *(Continued)*

	• Sudden onset
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Olivar Lopez 2020 *(Continued)*

DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Unclear risk

Peng 2020

Study characteristics	
Patient Sampling	**Purpose:** analyse the clinical features and imaging manifestations of COVID-19 **Design**: cross-sectional, single-centre, retrospective study **Recruitment:** clinically suspected cases who were sent to hospital for screening **Sample size:** n = 86 (n = 11) **Inclusion criteria**: clinically suspected patients **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR via nasopharyngeal swab **Facility controls**: negative RT-PCR via nasopharyngeal swab (once) **Country:** China **Dates**: 23 January 2020-16 February 2020 **Symptoms and severity**: fever, cough, dyspnoea, sore throat, fatigue, systemic soreness, runny nose **Demographics**: M/F: total 39/47, cases: 5/6, controls 34/40 Case group: mean age 40.73 ± 11.32 years, 5 men. Control group: mean age 39.67 ± 13.90 years, 34 men **Exposure history**: 7/11 COVID-19 patients (63.6%) had a history of travel to Hubei (5 Wuhan, 1 Huanggang, 1 Xiaogan), 2 patients had close contact with the COVID-19 patients, and 2 taxi drivers
Index tests	• Fever • Cough • Dyspnoea • Sore throat • Fatigue • Systemic soreness • Runny nose

Peng 2020 *(Continued)*

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swab)
Flow and timing	Time interval not specified
Comparative	
Notes	Funding: supported by the Key Discipline of Pudong Area, Shangai

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Peng 2020 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Peyrony 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to assess utility of clinical parameters, physician clinical judgment, and lung ultrasonography to accurately identify SARS-CoV-2-infected patients at ED presentation **Design**: prospective cohort study **Recruitment:** cohort of all adult (≥ 18 years) patients with suspected COVID-19 who were tested for SARS-CoV-2 prospectively enrolled at university ED (not every patient was tested for SARS-CoV-2: testing was left to the clinician's discretion) **Sample size:** n = 391 (225 cases) **Inclusion criteria**: no predefined inclusion criteria. Testing was mostly performed in patients who had severe symptoms such as dyspnoea, reported shortness of breath, presented with comorbidities, or were > 70 years. Some patients without COVID-19 symptoms were also tested when they needed admission to hospital. **Exclusion criteria**: patients who attended the ED more than once (only the last visit was included). There were no other exclusion criteria.
Patient characteristics and setting	**Facility cases:** all patients who tested positive for SARS-CoV-2 by RT-PCR **Facility controls**: all patients who tested negative for SARS-CoV-2 by RT-PCR **Country:** France **Dates**: 09 March 2020-04 April 2020 **Symptoms and severity**: moderate to mild severity, inclusion based on signs and symptoms suggestive of SARS-CoV-2 infection, 82% of included patients with comorbidities; not all included patients had COVID-19 symptoms **Demographics**: all included patients (pos + neg): median age: 62 years % female: 38.4% **Exposure history**: not specified
Index tests	• Fever • Cough • Dyspnoea • Myalgia

Peyrony 2020 *(Continued)*

	• Rhinitis/pharyngitis • Anosmia • Headache • GI symptoms • Fatigue • Chest pain • Dizziness/syncope • Haemoptysis • Oxygen saturation
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR for SARS-CoV-2 (negatives re-tested after 48 h), nasal swab
Flow and timing	RS and index tests both taken at presentation
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			

Peyrony 2020 *(Continued)*

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Pisapia 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to compare the characteristics at hospital admission of confirmed and not-confirmed COVID-19 patients, in the early phase of the epidemic **Design**: retrospective cohort study **Recruitment:** all patients consecutively admitted in selected medical wards (ED + lab) of the mono-specialist infectious diseases referral centre because of clinical suspicion of COVID-19 **Sample size:** n = 37 (17 cases) **Inclusion criteria**: all patients consecutively admitted in the selected medical wards because of clinical suspicion of COVID-19. No specification of 'suspicion' **Exclusion criteria**: none
Patient characteristics and setting	**Facility cases:** suspected cases with a positive RT-PCR (second test after 24 h if first negative) **Facility controls**: suspected cases with a negative RT-PCR (2 negative tests) **Country:** Italy **Dates**: 10 February 2020-10 March 2020 **Symptoms and severity**: mild to moderate severity

Pisapia 2020 *(Continued)*

	Demographics: median age cases: 49 years controls: 29 years. Gender: % female cases: 35%, controls: 35% **Exposure history**: travel to affected area: cases 35%, controls 95%. Contact with a confirmed case: cases 47%, controls: 0%. Contact with people from affected area: cases: 12% controls: 0%
Index tests	• Fever • Cough • Dyspnoea • Arthralgia • Conjunctivitis • Other
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, different tests used: targeted to different genomic region (regions RdRp, N and E) (commercial kits used during study changed), negatives re-tested after 24 h, nasopharyngeal swab
Flow and timing	RS and index tests both taken on admission
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	

Pisapia 2020 *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Pivetta 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of COVID-19 pneumonia; to explore whether the integration of lung ultrasound and clinical evaluation increases the sensitivity of the diagnosis of COVID-19 pneumonia **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all adult patients visiting an ED and screened positive for SARS-CoV-2-associated symptoms **Sample size:** n = 228 (107 cases) **Inclusion criteria**: all adults (≥ 18 years) who screened positive for acute symptoms associated with SARS-CoV-2 infection at triage (= fever, dyspnoea, new or worsening cough, sore throat, diarrhoea, ageusia, anosmia and asthenia) **Exclusion criteria**: patients known to be infected by SARS-CoV-2, requiring an urgent psychiatric assessment, or already intubated at arrival, no attending physician with expertise in lung ultrasonography available
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2, 1 test in patients with an initial positive PCR result, 2 tests in patients with an initial negative PCR result when clinical, sonographic, lab or imaging results were suggestive of COVID-19

Pivetta 2020 *(Continued)*

	Facility controls: negative RT-PCR test for SARS-CoV-2 and all other test results are concordant **Country:** Italy **Dates**: 01 April 2020-20 April 2020 **Symptoms and severity**: ED outcome: home discharge 25.2% cases, 78.5% controls, ward admission 60.8% cases, 20.7% controls, ICU admission 7.5% cases, 0.8% controls, ED death 6.5% cases, 0% controls **Demographics**: age: controls median 50.3 years, cases median 62.8 years M%/F%: cases 54.1/45.9, controls 43.7/56.3 **Exposure history**: not specified
Index tests	• Ageusia • Anosmia • Cough • Diarrhoea • Fatigue • Fever • Headache • Shortness of breath • Sore throat
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swabs), and in some cases other information including clinical, lab, imaging
Flow and timing	Maximum 72 h between index tests and RS
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			High

Pivetta 2020 *(Continued)*

DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			High
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		High risk	

Pokorska-Śpiewak 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to compare clinical severity and epidemiological spectrum between COVID-19 and influenza in children **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all consecutive paediatric patients referred to a tertiary healthcare department **Sample size:** n = 319 (15 cases)

Pokorska-Śpiewak 2021 *(Continued)*

	Inclusion criteria: clinical symptoms (WHO definition) of the disease or positive epidemiological history (international travel or contact with infected person) **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Poland **Dates**: 01 February 2020-15 April 2020 **Symptoms and severity**: mild to moderate severity, hospitalisation needed in 73% of cases and 37% of controls, none needed mechanical ventilation **Demographics**: age: controls median 84 months, cases median 128 months M%/F%: cases 53.3/46.7, controls 50.7/49.3 **Exposure history**: household contacts with confirmed positive patient: 100% of cases, 9.2% of controls; history of travel: 6.7% of cases, 25.3% of controls
Index tests	• Fever • Cough • Shortness of breath • Diarrhoea • Vomiting • Rhinitis • Abdominal pain • Sore throat • Headache • Myalgia • Chest pain • Fatigue • Conjunctivitis • Skin rash
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swabs)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Pokorska-Śpiewak 2021 *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Porto 2021

Study characteristics			

Porto 2021 *(Continued)*

Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to identify the symptoms associated with early stage SARS-CoV-2 (COVID-19) infections in HCWs using both clinical and laboratory data **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all patients presenting themselves at a polyclinic (a designated diagnostic site for personnel working in the Brazilian public health system, for screening of COVID-19) **Sample size:** n = 1297 (410 cases) **Inclusion criteria**: all patients presenting at the Piquet Carneiro Polyclinic, test indication not specified, but high proportion of symptomatic individuals in recruited population **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative or inconclusive RT-PCR test for SARS-CoV-2 **Country:** Brazil **Dates**: 19 March 2020-08 April 2020 **Symptoms and severity**: not specified, mostly symptomatic presentation (mild to moderate severity) **Demographics**: age: overall 42 years M%/F%: overall 28.2/71.8 **Exposure history**: confirmed contact with SARS-CoV-2 infected person: 43.8% of cases 43.3% in controls
Index tests	• Cough • Headache • Body ache • Fever • Sore throat • Coryza • Tiredness • Sneeze • Nasal congestion • Prostration • Respiratory difficulty • Diarrhoea • Anosmia or hyposmia • Chills • Anxiety • Nausea of vomiting • Eye conjunctiva congestion • Palpitations • Irritability • Abdominal pain • Sputum production • Difficulty swallowing

Porto 2021 *(Continued)*

	• Mental confusion • Lymph node enlargement • Skin rash
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swabs)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: the Laboratory of Histocompatibility and Cryopreservation received a thermo cycler and a −80 °C freezer from COVID-19 donation open account for Pedro Ernesto University Hospital. Rio de Janeiro Health Secretary provided nucleic acid extraction and RT-PCR

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		

Porto 2021 *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Raberahona 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to identify clinical signs and symptoms and epidemiological features that could help discriminate confirmed cases of COVID-19 from SARS-CoV-2-negative patients **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** patients visiting the screening centre **Sample size:** n = 3154 (1288 cases) **Inclusion criteria**: patients visiting the screening centre **Exclusion criteria**: PCR unknown or inconclusive result
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Madagascar **Dates**: 06 May 2020-01 July 2020 **Symptoms and severity**: mostly mild to moderate severity, 27.8% asymptomatic **Demographics**: age: controls median 31 years, cases median 39 years M%/F%: cases 48.6/51.4, controls 51.1/48.9

Raberahona 2020 *(Continued)*

	Exposure history: self-reported contact cases 19.2%, controls 26.2%
Index tests	• Fever or history of fever • Cough • Haemoptysis • Sore throat • Rhinorrhoea • Otalgia • Ageusia • Anosmia • Nasal obstruction • Abdominal pain • Wheezing • Chest pain • Myalgia/arthralgia • Malaise/fatigue • Dyspnoea • Headache • Nausea/vomiting • Diarrhoea • Signs of pneumonia • Acute respiratory distress
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR, nasopharyngeal swabs
Flow and timing	Not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			

Raberahona 2020 *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		High risk	

Romero-Gameros 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to determine the diagnostic yield of a self-assessment questionnaire on smell alterations and the psychophysical olfactory test as screening instruments for COVID-19 **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** patients who sought a respiratory triage assessment at ED of tertiary care hospital due to COVID-19 suspicion **Sample size:** n = 139 (72 cases) **Inclusion criteria**: > 18 years, nasopharyngeal swab taken, present with mild to moderate form of the disease

Romero-Gameros 2020 *(Continued)*

	Exclusion criteria: > 65 years, Parkinson or Alzheimer's history, chronic rhino sinusitis, allergic rhinitis, no SARS-CoV-2 PCR result, requiring hospitalisation
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Mexico **Dates**: 25 May 2020-30 June 2020 **Symptoms and severity**: mild to moderate severity, patients in need of hospitalisation were excluded **Demographics**: age: controls mean 39.2 years, cases mean 38.9 years M%/F%: cases 37.5/62.5, controls 35.8/64.2 Medium-high academic level: 99% **Exposure history**: not specified
Index tests	• Headache • Abdominal pain • Cough • Asthenia • Fever • Myalgia • Arthralgia • Conjunctivitis • Diarrhoea • Rhinorrhoea • Dysosmia • Nasal obstruction • Hyposmia - anosmia • Odynophagia • Dysgeusia (Self-assessment questionnaire of smell disorders, pocket smell test)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swabs)
Flow and timing	RS taken at presentation, after ENT team assessment of symptoms
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Romero-Gameros 2020 *(Continued)*

Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Romero-Gameros 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to evaluate and establish the diagnostic performance of symptoms and signs in patients with suspected COVID-19 **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** patients who came to the ED for suspected COVID-19. Patients were selected through a non probabilistic sampling of consecutive cases according to the order of arrival at the ED **Sample size:** n = 2137 (1148 cases) **Inclusion criteria**: > 17 years, high clinical probability of SARS-CoV-2, confirmatory RT-PCR available **Exclusion criteria**: no RT-PCR test done
Patient characteristics and setting	**Facility cases:** positive RT-PCR test for SARS-CoV-2 **Facility controls**: negative RT-PCR test for SARS-CoV-2 **Country:** Mexico **Dates**: 14 April 2020-21 July 2020 **Symptoms and severity**: mild to moderate severity, high prevalence (> 50%) of symptoms such as cough, asthenia, myalgia and headache; oxygen saturation < 93% in 11% of cases and 4% of controls **Demographics**: age: controls mean 42.8 years, cases mean 48.6 years M%/F%: cases 55.7/44.2, controls 46.8/53.1 **Exposure history**: not specified
Index tests	• Fever (> 38 °C) • Cough • Odynophagia • Thoracic pain • Aesthenia • Myalgia • Rhinorrhoea • Headache • Anosmia • Conjunctivitis • Dyspnoea • Temperature • Heart rate • Respiratory rate • Systolic BP • Diastolic BP • Oxygen saturation (median) • Oxygen saturation < 93%
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swabs)

Romero-Gameros 2021 *(Continued)*

Flow and timing	Timing not specified
Comparative	
Notes	Funding: supported by the Mexican Institute of Social Security

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	No		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		

Romero-Gameros 2021 *(Continued)*

Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Rutten 2020a

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); describing (a)typical symptoms and disease course in confirmed COVID-19 patients **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all patients in a nursing home that were suspected of COVID-19 underwent a diagnostic test **Sample size:** n = 1969 (857 cases) **Inclusion criteria**: patients with at least 2 of the following symptoms: fever/feverish feeling, cough and shortness of breath - later on (from 10 April 2020) patients with atypical symptoms were added. **Exclusion criteria**: patients who didn't undergo a diagnostic test. Patients with unknown results
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** the Netherlands **Dates**: 18 March 2020-15 April 2020 **Symptoms and severity**: mild, moderate and severe cases, 30-day mortality almost 50% in the cases **Demographics**: mean age: cases 84 years, controls 83 years M%/F%: cases 35.0/65.0, controls 39.0/61.0 **Exposure history**: not specified
Index tests	• Cough • Fever • Shortness of breath • Confusion • Sore throat
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (specimen not specified), execution and analysis of a RT-PCR test differed per nursing home organisation
Flow and timing	Timing not specified

Rutten 2020a *(Continued)*

Comparative			
Notes	Funding: none declared		
Methodological quality			
Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		

Rutten 2020a *(Continued)*

Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

Rutten 2020b

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); describing (a)typical symptoms and disease course in confirmed COVID-19 patients **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all patients in a nursing home that were suspected of COVID-19 (based on the physician's assessment) **Sample size:** n = 4007 (1538 cases) **Inclusion criteria**: all nursing home residents with a clinical suspicion of COVID-19 based on the physician's assessment and for whom they had the result of the RT-PCR **Exclusion criteria**: residents of whom results of follow-up diagnostics were not (yet) available
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** the Netherlands **Dates**: 18 March 2020-13 May 2020 **Symptoms and severity**: decreased oxygen saturation in 44% of cases and 47% of controls, 30- day mortality 3 times higher in cases (42%) than in controls **Demographics**: mean age: cases 84 years, controls 83 years M%/F%: cases 36.0/64.0, controls 39.0/61.0 **Exposure history**: not specified
Index tests	• Cough • Shortness of breath • Fever • Sore throat • Delirium or confusion or drowsiness • Fatigue • Diarrhoea • Malaise • Rhinorrhoea • Nausea/vomiting • Common cold • Decreased oxygen saturation • Temperature (categories)

Rutten 2020b *(Continued)*

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (specimen not specified)
Flow and timing	Index tests and RS taken at same visit
Comparative	
Notes	Data overlap with Rutten 2020a Funding: supported by the Dutch Ministry of Health, Welfare, and sport

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Rutten 2020b *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Sacks 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to determine whether and which specific symptoms are associated with a positive COVID-19 test result **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** mandatory, large-scale programme with onsite capacity to test all HCWs with acute symptoms that were potentially consistent with COVID-19 on an outpatient basis **Sample size:** n = 1747 (157 cases) **Inclusion criteria**: all HCWs with symptoms including fever, myalgia, GI symptoms, runny nose, cough, shortness of breath, sore throat, and anosmia **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Massachusetts, USA **Dates**: 13 March 2020-02 April 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: mean age overall cohort: 39 years M%/F%: cases 32.0/68.0, controls 26.0/74.0 **Exposure history**: 69% reported direct patient contact as part of their routine work, 15% reported known contact inside or outside the hospital with someone who had been diagnosed with COVID-19
Index tests	• Anosmia • Fever • Myalgia • Nausea or vomiting or diarrhoea • Runny nose • Cough • Shortness of breath

Sacks 2020 *(Continued)*

	• Sore throat
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasopharyngeal swab)
Flow and timing	Timing not specified
Comparative	
Notes	Funded by Mass CPR Grant and the Massachusetts General Hospital Executive Committee on Research (Carney Family Foundation Award to CAS and Steve and Deborah Gorlin Research Scholars Award to RPW).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Sacks 2020 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Saegerman 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to develop a clinical decision support tool for diagnosis of COVID-19 in hospitals **Design**: cross-sectional cohort study, prospective data collection **Recruitment:** all patients directed to the triage centres of 2 university hospital EDs **Sample size:** n = 2152 (573 cases) **Inclusion criteria**: all suspected patients directed to the triage centres (no definition of 'suspected') **Exclusion criteria**: patient with missing data in clinical records or missing RT-PCR result
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Belgium **Dates**: 02 March 2020-15 June 2020 **Symptoms and severity**: not specified, clinical suspicion at presentation **Demographics**: mean age: cases 58 years, controls 52 years M%/F%: cases 48.7/51.3, controls 42.2/57.8 **Exposure history**: not specified
Index tests	• Dyspnoea • Chest pain • Rhinorrhoea • Sore throat • Dry cough

Saegerman 2021 *(Continued)*

	• Wet cough • Diarrhoea • Headache • Myalgia • Fever • Anosmia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (specimen not specified)
Flow and timing	Index tests and RS both taken at presentation
Comparative	
Notes	Funded by the Liège University Hospital

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Saegerman 2021 *(Continued)*

Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk
Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Salmon Ceron 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); second part of the study: to assess the diagnostic accuracy of olfactory/gustatory dysfunction for SARS-CoV-2 infection in the overall population tested for SARS-CoV-2 **Design**: prospective cohort study **Recruitment:** all consecutive patients who were tested for SARS-CoV-2 in the Paris-based screening centre for COVID-19 **Sample size:** n = 1824 (849 cases) **Inclusion criteria**: (second part of the study): all consecutive patients with a suspicion of SARS-CoV-2 infection, independent of loss of smell no specification of 'suspicion' **Exclusion criteria**: (second part of the study): none
Patient characteristics and setting	**Facility cases:** all suspected patients with a positive RT-PCR **Facility controls**: all suspected patients with a negative RT-PCR **Country:** France **Dates**: 17 March 2020-25 March 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: not specified for second part of this study **Exposure history**: not specified
Index tests	• Self-reported loss of smell and/or taste: loss of smell only, loss of taste only, loss of smell and taste, loss of smell and/or loss of taste • Cough • Headache

Salmon Ceron 2020 *(Continued)*

	• Sore throat		
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR test, nasopharyngeal swabs		
Flow and timing	RS and index tests both taken at presentation		
Comparative			
Notes	Funding: none declared		
Methodological quality			
Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Salmon Ceron 2020 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Shah 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe characteristics, diagnostics and outcomes of patients with respiratory illness, comparing patients with and without COVID-19 disease **Design**: retrospective cohort **Recruitment:** all patients presenting to an ED with an acute respiratory illness and tested for SARS-CoV-2 **Sample size**: n = 316 (33 cases) **Inclusion criteria**: all patients ≥ 18 years who underwent testing for COVID-19 within 24 h of presentation to the ED. Patients with acute respiratory symptoms, influenza-like illness **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** California, USA **Dates**: 03 February 2020-31 March 2020 **Symptoms and severity**: not specified **Demographics**: median age: cases 63, controls 62. %. Female: cases 36%, controls 50% **Exposure history**: travel in last 21 days or known COVID exposure: cases 46%, controls 11%
Index tests	• Fever (patient-reported) • Fatigue/malaise • Cough (dry, productive) • Myalgia • Dyspnoea • Chest pain • Sore throat • Nasal congestion/rhinorrhoea • Diarrhoea

Shah 2020 *(Continued)*

	• Nausea • Vomiting • Abdominal pain • Headache • Altered mental status • Tachycardia (> 100 beats/min) • Low mean arterial pressure (< 60 mmHg) • Tachypnoea (respiratory rate > 20 breaths/min) • Fever
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR test, oropharyngeal and/or nasopharyngeal swabs
Flow and timing	RS performed maximum 24 h later than index tests
Comparative	
Notes	Funding: supported by the National Center for Advancing Translational Sciences, the National Heart Lung Blood Institute, National Institute of Allergy and Infectious Diseases, the Chan Zuckerberg Biohub, the Chan Zuckerberg Initiative

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern

Shah 2020 *(Continued)*

DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Simpson 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the demographics, clinical features, and test results of children referred from their primary provider for SARS-CoV-2 testing in the community setting **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** all children (0-22 years) who were referred by paediatricians to an outpatient paediatric testing site **Sample size:** n = 1210 (378 cases) **Inclusion criteria**: children presenting with mild symptoms, children who were at high risk for serious infection, children who lived with high-risk household members, or children who lived with household members whose work status would be impacted by the presence of infection **Exclusion criteria**: patients were excluded from the geospatial analysis if they had invalid addresses (n = 12)
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** USA **Dates**: 21 March 2020-16 May 2020

Simpson 2020 *(Continued)*

	Symptoms and severity: mostly mild symptoms **Demographics**: median age overall: 8 years M%/F%: cases 47.6/49.3 controls: 52.0/47.8 **Exposure history**: not specified, self-reported high-risk contacts vs no high-risk contacts: OR = 1.6
Index tests	• Uupper respiratory tract symptoms (e.g. sore throat or nasal congestion) • Cough • Lower respiratory tract symptoms (e.g. difficulty breathing) • GI symptoms (e.g. vomiting or diarrhoea) • Neurologic symptoms (e.g. headache) • Systemic symptoms (e.g. fever)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (naso- or oropharyngeal swab)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	

Simpson 2020 *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Unclear risk	

Sonoda 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to investigate the clinical symptoms to discriminate between COVID-19 and non-COVID-19 cases among outpatients in GP clinics **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** outpatients visiting the screening centre (GP clinic) **Sample size:** n = 360 (17 cases) **Inclusion criteria**: patients visiting the centre with suspicion of COVID-19 (no definition of 'suspicion') **Exclusion criteria**: patients who didn't receive a RT-PCR test
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Japan **Dates**: 01 August 2020-14 August 2020 **Symptoms and severity**: clinical spectrum of cases (n = 17) was 14 moderate, 2 moderate and 1 severe illness

Sonoda 2021 *(Continued)*

	Demographics: mean age: cases 39.6 years, controls 41.2 years M%/F%: cases 58.8/41.2, controls 50.7/49.2 **Exposure history**: close contact to patients with COVID-19: cases 13.3%, controls 8.1%
Index tests	• Body temperature • Headache • Sore throat • Dysgeusia • Anosmia • Nasal discharge • Cough • Sputum production • Nausea/vomiting • Diarrhoea • Stomach ache • Fatigue • Shortness of breath • Joint pain • Myalgia • Lack of appetite
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasal swab or saliva specimen)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			

Sonoda 2021 *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Sun 2020

Study characteristics	
Patient Sampling	**Purpose:** algorithm development for estimating risk of COVID-19 **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** patients presenting at the designated national outbreak screening centre and tertiary care hospital in Singapore for SARS-CoV-2 testing. Patients were either self-referred, referred from primary care facilities, or were at-risk cases identified by national contact tracing efforts (recruited n = 991) **Sample size:** n = 788 (n = 54) **Inclusion criteria**: patients presenting to the centre: • self-referred • referred from primary care facilities • at-risk cases identified by national contact tracing efforts

Sun 2020 *(Continued)*

	Exclusion criteria: PCR results not available at time of data collection - no electronic medical records - unavailable vital sign records
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 RT-PCR test **Facility controls**: all SARS-CoV-2 RT-PCR results were negative (minimum 2 test negatives in high-risk patients, minimum 1 test low-risk patients) **Country:** Singapore **Dates**: 26 January 2020-16 February 2020 **Symptoms and severity**: 252 (33.2%) symptoms > 5 days at presentation, 75 (9.5%) any comorbidity **Demographics**: median age 34 years, range 7 years-98 years, IQR 27-45; cases median 42 years, range 16-79; controls 34 years, range 7-98 M/F: 48.3%/51.7% F (cases M: 88 (88.9%)) **Exposure history**: contact with a known COVID-19 case (20.1% (32/54 cases (59.3%)); 126/734 controls (17.2%), contact with travellers from China (22.1%, 15/54 cases (27.8%); 42/734 controls (5.7%)), recent travel history, and visit to hospital in China within 14 days prior to symptom onset (0.8%)
Index tests	• Body temperature • Heart rate • Respiratory rate • Systolic BP • Diastolic BP • Cough • Sputum production • Shortness of breath • Rhinnorhea or nasal congestion • Sore throat • Auscultation finding of pneumonia • Other respiratory symptoms • GI symptoms
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2, 2 commercial assays 2-target (1 assay: Orf1ab and N - other unclear) RT-PCR
Flow and timing	Time interval not specified
Comparative	
Notes	Funding: supported by the following grants from Singapore Ministry of Health's National Medical Research Council: collaborative Solutions Targeting Antimicrobial Resistance Threats in Health Systems (CoSTAR-HS) [NMRC CGAug16C005], NMRC Clinician Scientist Award [MOH-000276] and NMRC Clinician Scientist Individual Research Grant [MOH-CIRG18nov-0006].

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Sun 2020 *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		

Sun 2020 *(Continued)*

Could the patient flow have introduced bias?	Low risk

Tan 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to describe the differences in clinical presentation between COVID-19 and other respiratory viruses and to determine independently associated clinical features with COVID-19 **Design**: cross-sectional multicenter cohort study, retrospective data collection **Recruitment**: all patients who fulfilled the hospital's COVID-19 suspect criteria were admitted and tested for both SARS-CoV-2 and non-SARS-CoV-2 respiratory viruses. The hospital's suspect criteria were based on a combination of clinical symptoms, and a constant changing criteria for a history of (international) travel based on the current epidemiological risks **Sample size:** n = 469 (287 cases) (18 asymptomatic patients excluded from the analysis) **Inclusion criteria**: patients who were positive for either SARS-CoV-2 or a non-SARS-CoV-2 respiratory virus **Exclusion criteria**: testing negative for both SARS-CoV-2 and a non-SARS-CoV-2 respiratory virus; co-infection of SARS-CoV-2 and another non-SARS-CoV-2 respiratory virus; asymptomatic patients (screening)
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 (2, if first was negative) **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Singapore **Dates**: 17 January 2020-15 April 2020 **Symptoms and severity**: mild to moderate severity, some severe to death **Demographics**: mean age: ≤ 30 years: cases 32.4%, controls 37.9%; 31-60 years: cases 56.1%, controls 48.9%; > 60 years: cases 11.5%, controls 13.2% M%/F%: cases 81.2/18.8, controls 56.6/43.4 **Exposure history**: exposure to possible COVID-19-positive case: cases 54%, controls 46.2% Exposure to confirmed COVID-19-positive case: cases 24.7%, controls 11%. Resides in foreign worker dormitory: cases 51.6%, controls 17%. Positive contact with a person with acute respiratory infection symptoms: cases 17.4%, controls 27.5%
Index tests	• Fever • Sore throat • Cough • Rhinorrhea or congested nose • Myalgia • Ansomia and/or dysgeusia • GI symptoms (including abdominal pain, nausea, vomiting diarrhoea) • Tachycardia (> 100 beats/min)

Tan 2021 *(Continued)*

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (oropharyngeal and/or nasopharyngeal swabs)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Tan 2021 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Unclear risk

Tolia 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of acute SARS-CoV-2 infection **Design**: cross-sectional cohort, retrospective data collection **Recruitment:** all patients presenting to 1 of 2 EDs, located at an urban teaching hospital, and academic quaternary medical centre, within the same healthcare system who had targeted testing based on clinician's decision during the initial 10 days of test availability **Sample size:** n = 283 (29 cases) **Inclusion criteria**: • patients presenting with symptoms related to COVID-19 infection (fever and cough or shortness of breath) • travel within 14 days to countries with high rates of infection (at that time China, Iran, Italy, Japan and South Korea) or • risk factors for infection complications (including age or comorbid conditions) or • the patient was a HCW who could potentially expose others at risk and clinician made decision for testing **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** positive SARS-CoV-2 test **Facility controls**: negative SARS-CoV-2 test, visiting the same EDs and being tested **Country:** USA (San Diego, CA) **Dates**: 10 March 2020-19 March 2020 **Symptoms and severity**: not specified, all patients presenting with symptoms related to COVID-19 infection (fever and cough or shortness of breath)

Tolia 2020 *(Continued)*

	Demographics: age (< 18 years: 0.7%, 18-64 years: 83.4%, > 65 years: 15.9%); gender: cases M/F%: 55.2/44.8; controls M/F%: 52.8/47.2; all M/F%: 53.0/47.0 **Exposure history**: recent travel (5.5%), 90.6% symptom-based criteria for testing, no known exposure history based
Index tests	• Fever
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: commercial RT-PCR test - ePLex SARS-CoV-2 test (nasopharyngeal swab)
Flow and timing	Probably no time interval between index test and RS, but not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			

Tolia 2020 *(Continued)*

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Tordjman 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of COVID-19 pneumonia; to determine the effectiveness of a pre-test probability score for SARS-CoV-2 infection **Design**: cross-sectional cohort, retrospective data collection **Recruitment:** a retrospective cohort of 200 patients with both RT-PCR and CT scan results available with a 1:1 patient:control inclusion ratio from ED at Cochin Hospital (Paris, France) with a suspicion of SARS-CoV-2 infection: 100 consecutive infected patients and 100 consecutive controls + a validation cohort: consecutive recruitment of outpatients suspected with COVID-19 (different from derivation cohort) at Cochin Hospital, Ambroise Paré and Raymond Poincaré hospitals **Sample size**: n = 605 (361) (no clinical data available from validation cohort) **Inclusion criteria**: clinical suspicion of SARS-CoV-2 infection, and both RT-PCR and CT scan available, 'suspicion' not defined **Exclusion criteria**: absence of confirmed diagnosis (diagnosis still under investigation; lack of blood test including complete white blood cell count and serum electrolytes; absence of reported clinical characteristics)
Patient characteristics and setting	**Facility cases:** suspected patients with a positive RT-PCR or positive CT scan (positive signs of COVID-19 pneumonia: usually bilateral and peripheral ground-glass and consolidated pulmonary opacities) **Facility controls**: suspected patients with a negative RT-PCR and negative findings on CT scan **Country:** France

Tordjman 2020 *(Continued)*

	Dates: 10 March 2020-30 April 2020 **Symptoms and severity**: not specified, mild to moderate severity **Demographics**: median age: cases 60.8 years, controls 54.1 years. Female %: cases 40%, controls 50% **Exposure history**: not specified
Index tests	• Cough • Fever • Shortness of breath • Diarrhoea • Myalgia • Headache • Anosmia • Ageusia
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection and COVID-19 pneumonia • RS: RT-PCR (specimen not specified) or CT scan lungs
Flow and timing	RS and index tests both taken at first presentation
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	No		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	

Tordjman 2020 *(Continued)*

Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Unclear		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Trubiano 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) **Design**: prospective cohort study **Recruitment:** data on all patients presenting at a COVID-19 rapid assessment screening clinic were prospectively collected in an electronic database. Only those patients who met the DHHS (Victorian Department of Health and Human Services) criteria for SARS-CoV-2 testing had nasopharyngeal swab collected for SARS-CoV-2 nucleic acid detection by PCR **Sample size:** n = 2935 (108 cases) **Inclusion criteria**: all people meeting DHHS criteria for testing: fever or chills in the absence of an alternative diagnosis that explains the clinical presentation or acute respiratory infection symptoms (e.g. cough, sore throat, shortness of breath, runny nose, loss of smell or loss of taste) **Exclusion criteria**: pending or intermediate results
Patient characteristics and setting	**Facility cases:** patients with suspected COVID-19 with a positive RT-PCR for SARS-CoV-2

Trubiano 2020 *(Continued)*

	Facility controls: suspected patients with a negative RT-PCR for SARS-CoV-2 **Country:** Australia **Dates**: 11 March 2020-22 April 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: median age: cases 51 years, controls 38 years. Female %: cases 49.1%, controls 64.1% **Exposure history**: overseas health facility exposure: cases 1.9%, controls 4.0%. Australian health facility exposure: cases 11.1%, controls 31.5%. Contact with known COVID-19-positive patient: cases 57.4%, controls 15.8%
Index tests	• Any fever • Fever > 38 °C • Subjective fever • Sore throat • Cough • Shortness of breath • Chest pain • Anosmia • Ageusia • Anosmia or ageusia • Coryza • Diahrroea • Other GI symptoms • Malaise/myalgia/arthralgia • Headache
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swab)
Flow and timing	RS and index tests both taken at presentation
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		

Trubiano 2020 *(Continued)*

Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Tudrej 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to diagnose SARS-CoV-2 infection in primary care settings based on signs and symptoms **Design**: cross-sectional cohort study, prospective data collection

Tudrej 2020 *(Continued)*

	Recruitment: recruitment in 2 clinical laboratories in Lyon (France) to which GPs refer patients with suspected COVID–19 for a nasopharyngeal smear (RT-PCR) **Sample size:** n = 816 (198 cases) **Inclusion criteria**: all consecutive patients referred by GPs for PCR testing **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** all suspected patients with a positive RT-PCR **Facility controls**: all suspected patients with a negative RT-PCR **Country:** France **Dates**: 24 March 2020-14 April 2020 **Symptoms and severity**: not specified **Demographics**: all included patients: median age: 45 years, % female: 65% **Exposure history**: not specified, 37% of participants were healthcare professionals
Index tests	• Anosmia or hyposmia • Ageusia or hypogeusia • Fever • Asthenia • Headache • Cough • Dyspnoea • Chest pain • Myalgia • Diarrhoea • Dry nose • Stuffy nose • Dry throat • Sore throat
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (nasopharyngeal swab)
Flow and timing	RS specimen taken right after index tests, at presentation
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Tudrej 2020 *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Van Loon 2021

Study characteristics			

Van Loon 2021 *(Continued)*

Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to identify early symptoms of SARS-CoV-2 infection among HCWs **Design**: single-centre, cross-sectional cohort study, prospective data collection **Recruitment**: all hospital HCWs self-reporting mild symptoms of an acute upper or lower respiratory tract infection were tested in a large non-academic hospital **Sample size:** n = 373 (185 cases) **Inclusion criteria**: HCWs with respiratory complaints and fever, according to the national guidelines for PCR-testing for SARS-CoV-2 by Sciensano, based on those of the WHO and the European Center for Disease Control (ECDC). **Exclusion criteria**: inconclusive PCR results
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 (2, if first was negative) **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Belgium **Dates**: 09 March January 2020-17 April 2020 **Symptoms and severity**: mild symptoms of an acute upper or lower respiratory tract infection **Demographics**: mean age: < 30 years: total 20.4%, controls 60.5%; 30-39 years: total 30.0 %, controls 41.4%; 40-49 years: total 27.3%, controls 49.5%; 50-59 years: total 17.4%, controls 56.9%; ≥ 60 years: cases 4.8%, controls 33.3% M%/F%: cases 53.1/46.9, overall 22.2/77.8 **Exposure history**: HCWs in a hospital with a high number of admitted COVID-19 patients
Index tests	• Cough • Sore throat • Runny or stuffy nose • Headache • Myalgia • Diarrhoea • Fatigue • Shortness of breath • Sneezing • Anosmia • Fever
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasopharyngeal swab)
Flow and timing	Timing not specified
Comparative	

Van Loon 2021 *(Continued)*

Notes	Funding: none declared		
Methodological quality			
Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		

Van Loon 2021 *(Continued)*

Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

Van Walraven 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to derive and assess a model to predict the risk of SARS-CoV-2 in community-based people **Design**: cross-sectional study, prospective data collection **Recruitment:** all people who were tested between 13 March and 21 April 2020 at a community-based COVID-19 testing centre **Sample size:** n = 9172 (571 cases) **Inclusion criteria**: presence of symptoms including rhinorrhoea; fever symptoms including rigor, chills, perceived fever, or documented fever at home or at the screening clinic; cough; and shortness of breath. Any infection risk factor including close contact with a person with known or presumed COVID-19 disease or recent travel outside of Canada. In the absence of these indications, HCWs (or people cohabiting with a HCW) were included if they had symptoms of sore throat, sputum production, or rhinorrhoea. In the event of extenuating circumstances or if the person was referred to the screening clinic by public health officials for testing **Exclusion criteria**: result not known, people with previous testing
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Canada **Dates**: 13 March 2020-21 April 2020 **Symptoms and severity**: severity not specified. Mostly symptomatic presentation: cough or shortness of breath was present in > 80% of cases and controls **Demographics**: mean age: cases 45.4 years, controls 42.5 years M%/F%: cases 44.5/55.5, controls 43.3/56.7 **Exposure history**: contact %: 72.5 cases, 47 controls travel %: 25.7 cases, 24.2 controls
Index tests	• Rhinorrhoea • Fever symptoms (temp > 38 °C at screening, feverishness, chills, rigor, temp > 38 °C at home) • chest symptoms (cough, shortness of breath) • multivariable prediction rule (combination of sex + HCW + contact with case + rhinorrhoea + chest symptoms (cough or dyspnoea) + recent travel + recent case detection rate + age)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasopharyngeal and throat swabs)

Van Walraven 2021 *(Continued)*

Flow and timing	Timing not specified, likely both at presentation		
Comparative			
Notes	Funding: none declared		

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Van Walraven 2021 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?		Low concern
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		Low risk

Vieceli 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to develop a tool to identify patients with higher probability of COVID-19 diagnosis at admission **Design**: cross-sectional cohort study, retrospective data collection **Recruitment**: the first 118 consecutive patients aged ≥ 18 admitted to the hospital due to suspected COVID-19 were assessed **Sample size:** n = 100 (29 cases) **Inclusion criteria**: aged ≥ 18 years and suspected of COVID-19 **Exclusion criteria**: patients discharged within 24 h of admission
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 (2, if first was negative) **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Brazil **Dates**: 17 March January 2020-10 April 2020 **Symptoms and severity**: mild to severe **Demographics**: mean age: cases 62 years, controls 54 years M%/F%: cases 51.7/48.3, controls 39.4/60.6 **Exposure history**: no patients in the negative group (controls) had travelled in the previous 3 weeks, compared to 8 (28.6%) patients in the confirmed (cases) group
Index tests	• Fever • Dyspnoea • Cough • Expectoration

Vieceli 2020 *(Continued)*

	• Chest pain • Headache • Myalgia • Asthenia • Upper respiratory tract symptoms • GI symptoms (not specified) • Respiratory distress
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasal and throat swabs)
Flow and timing	Index tests and reference standard both on admission
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		

Vieceli 2020 *(Continued)*

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Vilke 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to assess the frequency of fever and other symptoms associated with COVID-19 among patients presenting to ED **Design**: cross-sectional study, retrospective data collection **Recruitment:** all patients presenting to 1 of 2 EDs, who were tested for acute COVID-19 while in the ED or within 2 h of their triage temperature **Sample size:** n = 6894 (330 cases) **Inclusion criteria**: all patients presenting to the ED who were tested for acute COVID-19 infection while in the ED or within 2 h of their triage temperature (if they were admitted and tested after they left the ED) **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive test on rapid antigen test for SARS-CoV-2 or positive RT-PCR for SARS-CoV-2 **Facility controls**: negative test on rapid antigen test for SARS-CoV-2 or negative RT-PCR for SARS-CoV-2 **Country:** USA (California) **Dates**: 10 March 2020-30 June 2020 **Symptoms and severity**: severity not specified. Mostly symptomatic presentation: cough was present in 64.5% of cases and 26.6% of controls, fever at presentation in 19.4% of cases and 5.6% of controls **Demographics**: not specified **Exposure history**: not specified

Vilke 2020 *(Continued)*

Index tests	• Presenting fever (≥ 38°C) • Cough • Recent fever or chills • Shortness of breath • Fatigue • Body aches • Nausea or vomiting • Sore Throat • Loss or change in taste or smell • Diarrhoea • Sinus problem • Headache • Presenting fever (≥ 38 °C) or recent fever/chills • Cough or presenting fever (≥ 38 °C) or recent fever/chills • Shortness of breath or cough or presenting fever (≥ 38 °C) or recent fever/chills • Fatigue or shortness of breath or cough or presenting fever (≥ 38°C) or recent fever/chills • Body aches or fatigue or shortness of breath or cough or presenting fever (≥ 38 °C) or recent fever/chills
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: rapid antigen test or SARS-CoV-2 RT-PCR test (nasal, nasopharyngeal and throat swabs)
Flow and timing	RS was taken within 2 h after the triage temperature
Comparative	
Notes	Funding: none declared

Methodological quality

Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			

Vilke 2020 *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Villerabel 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to evaluate the diagnostic value of a semi-objective olfactory test in patients with self-reported chemosensory dysfunction before COVID-19 testing; to describe the diagnostic value of suggestive patient-reported COVID-19 symptoms **Design**: cross-sectional study, prospective data collection **Recruitment:** all HCWs and adult patients presenting themselves at the COVID-19 screening facility of the university hospital of Montpellier **Sample size:** n = 809 (58 cases)

Villerabel 2021 *(Continued)*

	Inclusion criteria: all HCW or outpatients with symptoms or with close contact with an index case presenting at the screening facility **Exclusion criteria**: prior chemosensory dysfunction, testing inability, or contraindications
Patient characteristics and setting	**Facility cases:** positive test on rapid antigen test for SARS-CoV-2 or positive RT-PCR for SARS-CoV-2 **Facility controls**: negative test on rapid antigen test for SARS-CoV-2 or negative RT-PCR for SARS-CoV-2 **Country:** France **Dates**: 23 March 2020-22 April 2020 **Symptoms and severity**: severity not specified. Mild to moderate symptoms: 42.0% of patients presenting were asymptomatic, most common symptoms were cough, fever, headache, signs of upper respiratory tract infection and fatigue **Demographics**: mean age: cases 43.6 years, controls 41.7 years M%/F%: cases 32.8/67.2, controls 25.8/74.2 **Exposure history**: 71.1% had contact with COVID-19 cases
Index tests	• Arthralgia • Chest pain • Cough • Rash • Dyspnoea • Fatigue • Fever • GI tract disorders • Headache • Myalgia • Upper respiratory tract infection • Olfactory dysfunction • Flavour (gustatory dysfunction) • Taste (gustatory dysfunction) • Olfactory dysfunction and/or gustatory dysfunction • CODA (Clinical Olfactory Dysfunction Assessment)
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasopharyngeal swabs)
Flow and timing	Index tests and RS within 10 min
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Villerabel 2021 *(Continued)*

Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
Could the patient flow have introduced bias?		Low risk	

Wee 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to analyse OTDs as a diagnostic criterion for COVID-19 **Design**: cross-sectional, prospective single-centre study **Recruitment:** all suspected cases presenting to the ED **Sample size:** n = 870 (cases = 154) **Inclusion criteria**: • presence of respiratory symptoms and suspicious epidemiological links or travel history or • new onset OTD **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR for COVID-19 **Facility controls**: negative RT-PCR for COVID-19 **Country:** Singapore **Dates**: 26 March 2020-10 April 2020 **Symptoms and severity**: loss of sense of smell/taste **Demographics**: not specified **Exposure history**: close contact of a confirmed COVID-19 case: cases 42/112, controls 37/679
Index tests	• Loss of sense of smell/taste
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR (oropharyngeal swabs)
Flow and timing	Time interval: same day
Comparative	
Notes	Funding: none declared

Methodological quality			
Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Yes		

Wee 2020 *(Continued)*

Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Wei 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); diagnosis of SARS-CoV-2 in outpatients visiting a fever clinic **Design**: retrospective cohort study **Recruitment:** all febrile patients visiting the fever clinic of Tongji Hospital **Sample size:** n = 936 (628 cases)

Wei 2020 *(Continued)*

	Inclusion criteria: all febrile patients visiting the fever clinic **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** all febrile patients with a positive RT-PCR for SARS-CoV-2 (tested twice in 24 h) **Facility controls**: all febrile patients with a negative RT-PCR for SARS-CoV-2 (tested twice in 24 h) **Country:** China **Dates**: 30 January 2020-04 February 2020 **Symptoms and severity**: cases: 88.1% mild, 11.5% severe, 0.5% critical; controls: 90.3% mild, 9.1% severe, 0.7% critical **Demographics**: median age: cases: 53 years, controls: 49 years. Gender: % female cases: 52.9%, controls: 53.9% **Exposure history**: not specified
Index tests	• Fever • Cough • Fatigue • Chest tightness • Muscle ache • Diarrhoea • Dysponea • Anorexia • Rhinobyon • Vomiting • Sore throat • Aversion to cold • Nausea • Hypersomnia • Expectoration • Dizziness • Xerostomia • Chest pain • Abdominal distention
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: RT-PCR twice with a 24-h interval (throat swab specimens from the upper respiratory tract)
Flow and timing	RS and index tests both taken at presentation
Comparative	
Notes	Funding: supported by the National Natural Science Foundation of China [Grants 81874149, 81974456, and 81530024]; the Clinical Research Physician Program of Tongji Medical College, Huazhong University of Science and Technology [Grant 5001540075]; SARS-CoV-2 Pneumonia Emergency Technology Public Relations Project [2020FCA009]
Methodological quality	

Wei 2020 *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		

Wei 2020 *(Continued)*

Could the patient flow have introduced bias?	Low risk

Wernhart 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to compare methods of outpatient management and testing strategies **Design**: cross-sectional study, prospective data collection **Recruitment:** all patients with respiratory symptoms reporting to 3 rural GP offices in North Rhine-Westphalia, Germany **Sample size:** n = 489; only 80 people RT-PCR tested (5 cases) **Inclusion criteria**: all patients from 3 GP offices reporting symptoms of respiratory tract infection **Exclusion criteria**: none specified, only 80 suspected patients tested of the 489, following the strict test criteria of the Robert Koch Institute (RKI)
Patient characteristics and setting	**Facility cases:** patients receiving a smear test according to the RKI criteria and testing RT-PCR-positive **Facility controls**: patients receiving a smear test according to the RKI criteria and testing RT-PCR-negative **Country:** Germany **Dates**: 27 January 2020-20 April 2020 **Symptoms and severity**: severity not specified. Mild to moderate symptoms: rhinopharyngitis in 40% and acute bronchitis in 60% of cases **Demographics**: mean age all patients 52.69 years; mean age of tested patients 47.03 years. Gender not specified **Exposure history**: not specified
Index tests	• Cough • Sore throat • Myalgia and fatigue • Headache • Rhinitis • Fever • Smell and taste dysfunction • Chills • Earache
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasopharyngeal swabs)

Wernhart 2020 *(Continued)*

Flow and timing	Index tests and RS both on the same day (patients referred directly to the smear centre)
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Yes		
Could the conduct or interpretation of the index test have introduced bias?		Low risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			

Wernhart 2020 *(Continued)*

Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
Could the patient flow have introduced bias?	Low risk

Xie 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of COVID-19 pneumonia; to compare the epidemiological, clinical, laboratory and radiological characteristics, treatment and outcomes between patients with confirmed COVID-19 pneumonia and those with suspected COVID-19 infection (71% of SARS-CoV-2-positive patients had CT-confirmed pneumonia) **Design**: retrospective 2-centre cohort **Recruitment:** patients in whom a RT-PCR test was performed at 2 Shangai hospitals **Sample size:** n = 105 (21 cases) **Inclusion criteria**: not specified **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** patients with a positive RT-PCR test for SARS-CoV-2 **Facility controls**: patients with a negative RT-PCR test for SARS-CoV-2 **Country:** China **Dates**: 01 January 2020-15 February 2020 **Symptoms and severity**: 72% of all participants were hospitalised, 71% of the cases had pneumonia, 88% of controls had pneumonia ("clinical symptoms usually mild") **Demographics**: mean age: cases: 54.0 years, controls: 41.6 years. Gender: % female cases: 38.1%, controls: 51.2% **Exposure history**: recently been to Wuhan: cases: 42.9%, controls: 17.9%. Contact with people from Wuhan: cases: 14.3%, controls: 0%. Recently been to supermarkets and groceries: cases: 28.6%, controls: 34.5%. Recently travelled: cases: 14.3%, controls: 47.6%
Index tests	• Fever • Cough • Sputum production • Myalgia • Weakness • Diarrhoea
Target condition and reference standard(s)	• TC: COVID-19 pneumonia

Xie 2020 *(Continued)*

- RS: RT-PCR testing on throat swab and sputum specimens, patients preselected on the presence of pneumonia (radiological findings)

Flow and timing	RS and index tests both taken at admission		
Comparative			
Notes	Funding: none declared		

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Unclear		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			High
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Xie 2020 *(Continued)*

DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Yes	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
Could the patient flow have introduced bias?		High risk

Yombi 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); diagnosis of SARS-CoV-2 infection, using clinical signs in HCWs **Design**: cross-sectional cohort study, retrospective data collection **Recruitment:** period 1: (before 30 March 2020) HCWs were tested only if they had fever and respiratory symptoms (some physicians were tested without fever); period 2 (after 30 March 2020), HCWs were tested if they had respiratory symptoms with or without fever **Sample size**: n = 536 (175 cases) **Inclusion criteria**: not specified (all suspected HCWs) **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** all suspected HCWs with a positive RT-PCR **Facility controls**: all suspected HCWs with a negative RT-PCR **Country:** Belgium **Dates**: 16 March 2020-24 April 2020 **Symptoms and severity**: not specified (from tables: mild to moderate severity) **Demographics**: % age < 45 years: cases: 56.6%, controls: 62.3% gender: % female cases: 67.4%, controls: 73.1% **Exposure history**: not specified (all HCWs)
Index tests	• Fever • Cough • Shortness of breath • Sore throat • Fever + cough • Fever + cough + shortness of breath • Fever + cough + sore throat
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection

Yombi 2020 *(Continued)*

	• RS: PCR for SARS-CoV-2 (sample not specified)
Flow and timing	Not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
Did the study avoid inappropriate inclusions?	Unclear		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			

Yombi 2020 *(Continued)*

Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
Could the patient flow have introduced bias?		Unclear risk

Yonker 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease) in children; to describe the paediatric impact of COVID-19, specifically focusing on viral burden, susceptibility to disease and immune responses **Design**: cross-sectional cohort study, retrospective data collection **Recruitment**: paediatric patients ≤ 22 years of age presenting to Infection Control clinics for medical evaluation of symptoms concerning for COVID-19 or admitted for acute symptoms related to COVID-19 or multisystem inflammatory syndrome in children (MIS-C) were offered enrolment in the paediatric COVID-19 bio repository **Sample size**: n = 174 (49 cases), excluding 18 MIS-C patients **Inclusion criteria**: children ages 0-22 years; symptoms concerning for COVID-19 or admitted for acute symptoms related to COVID-19 or MIS-C; informed consent, and if appropriate, assent,were verbally obtained by the patients or parent/guardian **Exclusion criteria**: none specified
Patient characteristics and setting	**Facility cases:** positive RT-PCR for SARS-CoV-2 **Facility controls**: negative RT-PCR for SARS-CoV-2 **Country:** Massachusetts, USA **Dates**: not stated (before 29 July 2020 (date of article submission)) **Symptoms and severity**: asymptomatic to mild symptoms to MIS-C **Demographics**: mean age: cases 12.7 years, controls 9.6 years M%/F%: cases 46.9/53.1, overall 53.6/46.4 **Exposure history**: household exposures cases: mother: 40.8%, father: 26.5%, sibling: 18.4%, other: 18.4%, no household exposure: 18.4% Household exposures controls: mother: 16.8%, father: 8.8%, sibling: 6.4%, other: 15.2%, no household exposure: 56.0%
Index tests	• Nasal congestion • Rhinorrhea • Anosmia or hyposmia • Headache • Myalgia or arthralgia • Sore throat • Cough

Yonker 2020 *(Continued)*

	• Fever • Rash • Nausea or vomiting • Diarrhoea • Anorexia • Chills • Dyspnoea • Fatigue • Dysgeusia • Altered mental status • Lymphadenopathy
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: SARS-CoV-2 RT-PCR test (nasopharyngeal or oropharyngeal swabs)
Flow and timing	Index tests and reference standard both taken at presentation
Comparative	
Notes	MIS-C patients were excluded for our analyses Funding: Supported by the National Heart, Lung, and Blood Institute (5K08HL143183 to L.Y.), the Cystic Fibrosis Foundation (YONKER18Q0 to L.Y.), the National Institute of Child Health and Human Development (K08 HD094638 [to A.N.] and R01HD100022 [to A.E.]), Mark and Lisa Schwartz (to J.L.), the National Institute of Diabetes and Digestive and Kidney Diseases (DK039773, DK072381 [to J.B.] and DK104344 [to A.F.]), the National Institute of Allergy and Infectious Disease (K24AI141036 to I.B.), the Centers for Disease Control and Prevention (U01CK000490 to E.R.), and the Department of Pediatrics and the Department of Obstetrics/Gynecology at Massachusetts General Hospital (to L.Y. and A.E.)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			

Yonker 2020 *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Low risk	

Zayet 2020a

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to compare the symptoms of patients with positive and negative SARS-CoV-2 RT-PCR results and to determine the sensitivity, specificity, positive predictive value and negative predictive value for each of these symptoms in regard to SARS-CoV-2 RT-PCR

Zayet 2020a *(Continued)*

	Design: retrospective cohort study **Recruitment:** all adult patients (≥ 18 years) who presented for possible COVID-19 at the outpatient department **Sample size:** n = 217 (95 cases) **Inclusion criteria**: all adult patients (≥ 18 years) who presented for possible COVID-19 at the outpatient department **Exclusion criteria**: pregnant women, children (< 18 years) and patients with dementia (unable to report functional symptoms)
Patient characteristics and setting	**Facility cases:** patients with suspected COVID-19 with a positive RT-PCR **Facility controls**: patients with suspected COVID-19 with a negative RT-PCR **Country:** France **Dates**: 30 March 2020-03 April 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: mean age: cases: 39.8 years, controls: 39.6 years. Gender: % female cases: 83.2%, controls: 86.9% **Exposure history**: not specified (mostly HCWs)
Index tests	• Fever • Myalgia/arthralgia • Headache • Cough • Dyspnoea • Dysgeusia • Anosmia • Rhinorrhea • GI symptoms
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: PCR for SARS-CoV-2 (nasopharyngeal swabs)
Flow and timing	Not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		

Zayet 2020a *(Continued)*

Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

Zhu 2020

Study characteristics	
Patient Sampling	**Purpose:** description of initial clinical features in patients with suspected and confirmed SARS-CoV-2 infection **Design**: cross-sectional cohort, retrospective data collection

Zhu 2020 *(Continued)*

	Recruitment: all patients with suspected COVID-19 who presented to the ED of the First Affiliated Hospital of USTC and the Infectious Hospital of the First Affiliated Hospital of USTC for the first time **Sample size:** n = 116 (32 cases) **Inclusion criteria**: • patients defined as suspected SARS-CoV-2 infection based on guidelines for the diagnosis and treatment of pneumonia caused by novel coronavirus infection (trial version III) • presentation to, clinical observation and quarantine in ED • nucleic acid amplification test performed in the ED **Exclusion criteria**: transfer from another hospital or previous visit to First Affiliated Hospital and previous diagnosis of COVID-19
Patient characteristics and setting	**Facility cases:** positive nucleic acid amplification test on admission or 24 h later **Facility controls**: SARS-CoV-2 PCR test negative **Country:** China, Anhui **Dates**: 24 January 2020-20 February 2020 **Symptoms and severity**: all suspected COVID-19 patients included; days since onset of symptoms median 5 (IQR 2-7) **Demographics**: median age: all: 40 years (IQR 27-53), cases: 46 years (IQR 35-52), controls: 35 years (IQR 27-53); gender distribution M%/F%: all 46/54, cases 47/53, controls 46/54 **Exposure history**: no specific exposure history common to all patients with suspected disease: 8 (25%) diagnosed patients had visited Wuhan in the previous 2 weeks and 12 (38%) had been exposed to patients with infection in the previous 2 weeks
Index tests	• Fever • Cough • Myalgia or fatigue • Expectoration • Chest stuffiness (congestion) • Haemoptysis • Headache • Diarrhoea
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: nucleic acid amplification test not further specified (twice in case-negatives) (samples: swabs, origin not specified)
Flow and timing	Index tests and RS both taken on admission or after 24 h
Comparative	
Notes	Funding: none declared
Methodological quality	

Zhu 2020 *(Continued)*

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Low risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Unclear risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		

Zhu 2020 *(Continued)*

Could the patient flow have introduced bias?	Unclear risk

Zimmerman 2020

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to develop a data-driven set of clinical indicators for COVID-19 that would help to identify outpatient symptoms and those who most benefit from limited testing availability **Design**: cross-sectional cohort study, prospective data collection **Recruitment: s**ymptomatic individuals who had either exposure to a case of COVID-19 or a typical respiratory illness symptom were scheduled at a centralised outpatient COVID-19 testing facility **Sample size:** n = 736 (55 cases) **Inclusion criteria**: either exposure to a case of COVID-19 or a typical respiratory illness symptom **Exclusion criteria**: asymptomatic individuals
Patient characteristics and setting	**Facility cases:** adult patients testing positive for SARS-CoV-2 infection **Facility controls**: adult patients testing negative for SARS-CoV-2 infection **Country:** Pennsylvania, USA **Dates**: 29 March 2020-26 April 2020 **Symptoms and severity**: mild to moderate severity **Demographics**: not specified **Exposure history**: contact with COVID-19 case: cases: 70%, controls: 21%
Index tests	• Fever • Chills • Cough • Sore throat • Shortness of breath • Muscle aches • Abdominal pain • Nausea/vomiting • Diarrhoea • Headache • Decrease or loss of taste or smell
Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: PCR for SARS-CoV-2 (specimen not specified)
Flow and timing	Not specified

Zimmerman 2020 *(Continued)*

Comparative	
Notes	Funding: supported through a co-operative agreement with the Centers for Disease Control and Prevention (CDC) through grant number U01 IP000467 and the National Institutes of Health grant number 1UL1 TR001857. The US Flu VE Network is supported through co-operative agreements funded by CDC.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		Unclear risk	
Are there concerns that the included patients and setting do not match the review question?			Unclear
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	Unclear		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	
Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern

Zimmerman 2020 *(Continued)*

DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Could the patient flow have introduced bias?	Unclear risk

Zurl 2021

Study characteristics	
Patient Sampling	**Purpose:** diagnosis of SARS-CoV-2 infection (mild COVID-19 disease); to analyse the infection rate in symptomatic children **Design**: cross-sectional cohort, retrospective data collection **Recruitment:** children presenting at university hospital's children's ED **Sample size:** n = 1105 (10 cases) **Inclusion criteria**: children with symptoms and anamnestic details according to national criteria for suspicion of SARS-CoV-2, and no alternative diagnosis **Exclusion criteria**: not specified
Patient characteristics and setting	**Facility cases:** SARS-CoV-2 PCR test-positive **Facility controls**: SARS-CoV-2 PCR test-negative **Country:** Austria **Dates**: 19 March 2020-15 August 2020 **Symptoms and severity**: not specified, mostly mild to moderate severity, 50% of cases requiring hospital admission, 32.4% of controls **Demographics**: median age: cases: 8.4 years, controls: 3.2 years gender M%/F%: cases 50/50, controls 52.1/47.9 **Exposure history**: known contact with a case: cases 0%; controls 1.4%

Index tests	• Sore throat
	• Respiratory signs and symptoms (all)
	  ○ laryngitis/hoarseness/stridor
	  ○ cough
	  ○ bronchitis/rhonchi
	  ○ dyspnoea/shortness of breath
	  ○ tachypnoea (age adapted)

Zurl 2021 *(Continued)*

	• Temperature ≥ 37.5 °C
	  ○ temperature ≥ 37.5 °C reported prior to admission
	  ○ temperature ≥ 37.5 °C measured at admission
	• Sudden onset of anosmia and or a-/-dysgeusia

Target condition and reference standard(s)	• TC: SARS-CoV-2 infection • RS: PCR for SARS-CoV-2 (naso- or oropharyngeal swabs)
Flow and timing	Timing not specified
Comparative	
Notes	Funding: none declared

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
Did the study avoid inappropriate inclusions?	Yes		
Could the selection of patients have introduced bias?		High risk	
Are there concerns that the included patients and setting do not match the review question?			Low concern
DOMAIN 2: Index Test (All tests)			
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
If a threshold was used, was it pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Low concern
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
Could the reference standard, its conduct, or its interpretation have introduced bias?		Low risk	

Zurl 2021 *(Continued)*

Are there concerns that the target condition as defined by the reference standard does not match the question?			Low concern
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
Could the patient flow have introduced bias?		Unclear risk	

BP: blood pressure; **CDC**: Centre for Disease Control; **COPD:** constructive obstructive pulmonary disease; **COVID-19:** coronavirus disease 2019; **CT:** computed tomography; **ED:** emergency department; **ENT:** ear, nose and throat; **F**: female; **FiO_2**: fraction of inspired oxygen; **GI:** gastrointestinal; **GP:** general practitioner; **HCW:** healthcare workers; **ICU:** intensive care unit; **IgM:** immunoglobulin M; **IQR:** interquartile range; **M:** male; **NCP:** novel coronavirus pneumonia; **OTD:** olfactory and taste disorder; **PaO_2**: partial pressure of oxygen; **POC:** point-of-care; **RS:** reference standard; **RT-PCR:** reverse transcription polymerase chain reaction; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **SD:** standard deviation; **SpO_2**: oxygen saturation; **TC:** target condition; **WBC:** blood white blood cell; **WHO:** World Health Organization; **2019-nCoV:** 2019 novel coronavirus

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Accorsi 2020	Ineligible population
Afshar 2020	Ineligible design
Agarwal 2021	Ineligible design
Ai 2020	Preprint
Akinbami 2021	Ineligible population
Akyala 2020	Ineligible population
Aleebrahim-Dehkordi 2020	Conference abstract
Al-Rifai 2021	Only SARS-CoV-2-positive patients
Altınbilek 2020	Ineligible outcomes
Andina-Martinez 2021	Only SARS-CoV-2-positive patients
Antonelli 2021	Index test not assessed on admission
Aubert 2021	Ineligible design
Auvinen 2021	Ineligible population
Baghaei 2020	Ineligible outcomes

Study	Reason for exclusion
Bailey 2020	No data
Bailey 2021	Ineligible outcomes
Bartlett 2020	Conference abstract
Bastiani 2021	Ineligible design
Bhatta 2021	Only SARS-CoV-2-positive patients
Bidkar 2021	Ineligible population
Bonadio 2020	Conference abstract
Brotons 2020	Preprint
Burrel 2021	Ineligible outcomes
Cadegiani 2021	Ineligible design
Cai 2020	Timing of index test not specified
Calagnan 2020	Ineligible design
Carignan 2020	Ineligible design
Challener 2020	Ineligible design
Chen 2020	Ineligible design
Chen 2021	Ineligible population
Concheiro-Guisan 2020	Index test not assessed on admission
D'Souza 2020	No clinical suspicion at inclusion
Dai 2021	Timing of index test not specified
Dantas 2021	Ineligible population
De Angelis 2020	Ineligible population
Deng 2020	Ineligible population
Dixon 2021	Index test not assessed on admission
Dreyer 2020	Ineligible population
Duan 2020	No data
Duque 2021	Ineligible design
Duramaz 2021	Only SARS-CoV-2-positive patients
Elimian 2020	Timing of index test not specified

Study	Reason for exclusion
Escosteguy 2020	Ineligible population
Feehan 2021	Ineligible population
Fisher 2021	Index test not assessed on admission
Foster 2021	Ineligible design
Gale 2020	Ineligible population
Gerkin 2021	Ineligible design
Giavedoni 2020	Only SARS-CoV-2-positive patients
Gibbons 2021	Index test not assessed on admission
Gnanasambantham 2020	Ineligible design
Goel 2020	Ineligible index test
Gombos 2021	No data
Goodacre 2020	Ineligible population
Guillén 2020	Only SARS-CoV-2-positive patients
Gurrola 2021	Only SARS-CoV-2-positive patients
Haddadin 2021	Ineligible population
Hamed 2021	Ineligible design
Hernández-Cruz 2021	Ineligible population
Hosseinzadeh 2021	Ineligible design
Hosseninasab 2020	Timing of index test not specified
Hubiche 2021	Conference abstract
Hurst 2020	No data
Indini 2021	Ineligible population
Islam 2020	Conference abstract
Jain 2021	Case report
Karni 2020	Ineligible design
Kasiukiewicz 2020	Conference abstract
Kline 2021	Ineligible design
Lechner 2021	Ineligible design

Study	Reason for exclusion
Lee 2020	Ineligible design
Lee 2021	Only SARS-CoV-2-positive patients
Li 2020a	Timing of index test not specified
Li 2020b	Timing of index test not specified
Li 2021	Ineligible outcomes
Liang 2020	Preprint
Liu 2021	Ineligible design
Loftus 2020	Index test not assessed on admission
Lu 2020	Ineligible population
Madan 2020	Ineligible design
Makaronidis 2020	Ineligible population
Manley 2020	Conference abstract
McDonald 2020	Ineligible design
McGovern 2020	Conference abstract
Medetalibeyoglu 2020	Conference abstract
Membrilla 2020	Only SARS-CoV-2-positive patients
Mizrahi 2020	Ineligible design
Möckel 2021	Ineligible design
Moolla 2021	Index test not assessed on admission
Muhammad 2021	Ineligible design
Munblit 2020	Only SARS-CoV-2-positive patients
Murillo-Zamora 2020	Ineligible index test
Nakajima 2021	Ineligible design
Nakanishi 2020	Ineligible design
Nayan 2021	No data
Nobel 2020	Ineligible design
Ortiz 2020	Only SARS-CoV-2-positive patients
Oshman 2020	Ineligible outcomes

Study	Reason for exclusion
Ozcan 2021	No data
Paar 2021	Ineligible population
Pigott 2020	Conference abstract
Platten 2021	No clinical suspicion at inclusion
Popovych 2021	Ineligible population
Pullen 2020	Ineligible design
Quer 2020	Ineligible design
Ravani 2020	No clinical suspicion at inclusion
Rentsch 2020	Preprint
Ronan 2021	No data
Rubel 2020	Index test not assessed on admission
Sabetian 2021	Only SARS-CoV-2-positive patients
Sabetta 2020	Ineligible outcomes
Sehanobish 2021	Index test not assessed on admission
Senok 2020	Ineligible design
Shanbehzadeh 2021	Ineligible design
Shayganmehr 2021	Ineligible population
Sheen 2020	No data
Shoer 2021	No clinical suspicion at inclusion
Sieber 2021	Ineligible population
Song 2020	Preprint
Sorlini 2020	Ineligible design
Spangler 2021	Ineligible outcomes
Stacevičienė 2021	Ineligible design
Tabacof 2020	Only SARS-CoV-2-positive patients
Taziki 2020	Index test not assessed on admission
Ticinesi 2020	Conference abstract
Trevisan 2021	Ineligible design

Study	Reason for exclusion
Verma 2020	Index test not assessed on admission
Viana dos Santos 2021	Ineligible design
Visconti 2021	Ineligible design
Vos 2020	Ineligible design
Weiss 2021a	Ineligible design
Weiss 2021b	Ineligible population
Wells 2020	No clinical suspicion at inclusion
Wu 2020	Only SARS-CoV-2-positive patients
Xia 2021	Ineligible population
Yan 2020	Ineligible design
Yang 2020	Preprint
Yousef 2021	Ineligible design
Žaja 2021	Only SARS-CoV-2-positive patients
Zavascki 2020	Preprint
Zayet 2020b	Ineligible design
Zhao 2020	Ineligible design
Zhao 2021	Ineligible design

DATA

Presented below are all the data for all of the tests entered into the review.

Table Tests. Data tables by test

Test	No. of studies	No. of participants
1 Cough	30	37427
2 Fever	29	44876
3 Dyspnoea	28	35258
4 Sore throat	26	30052
5 Headache	23	27042

Test	No. of studies	No. of participants
6 Diarrhoea	23	26155
7 Myalgia	19	16759
8 Anosmia	20	20108
9 Fatigue	19	14482
10 Chills/shivers	13	22559
11 Chest tightness/pain	13	20022
12 Rhinorrhea	12	24117
13 Ageusia	10	12937
14 Anosmia or ageusia	7	7966
15 Abdominal pain	7	7733
16 Nasal congestion	7	2837
17 Altered mentation/confusion	5	10073
18 Conjunctivitis	6	9187
19 Nausea or vomiting	5	5298
20 Gastrointestinal symptoms (not specified)	5	5184
21 Rash	5	2864
22 Coryza	4	10303
23 Sputum production/productive cough	5	7753
24 Asthenia	4	7410
25 Odynophagia	4	4053
26 Anosmia and ageusia	4	3003
27 Arthralgia	4	1753
28 Vomiting	4	1541
29 Wheeze	3	5597
30 Nausea	3	5527
31 Dry cough	3	3432
32 Malaise	3	2392
33 Enlargement of lymph nodes	3	6256

Test	No. of studies	No. of participants
34 Anosmia or hyposmia	3	1580
35 Anorexia	3	827
36 Fever (subjective)	3	12703
37 Haemoptysis	2	5206
38 Earache	2	4895
39 Systemic soreness (malaise/myalgia/arthralgia)	2	4202
40 High fever (≥ 38.5 °C)	2	3015
41 Myalgia or arthralgia	3	6764
42 Irritability	2	1777
43 Sneezing	2	1638
44 Anosmia or dysgeusia	2	1574
45 Loss of appetite	2	1345
46 Pulmonary auscultation: crackling bilateral	2	987
47 Sweating	2	915
48 Nasal symptoms	2	684
49 Rhinitis	2	399
50 Dysgeusia	2	313
51 SCRiPS score, recent case detection rate	1	9172
52 SCRIPS score, 0.5*recent case detection rate	1	9172
53 Rigors	1	9172
54 Cough or dyspnoea	1	9172
55 Dysuria	1	4815
56 Seizure	1	4815
57 Exanthema	1	4815
58 Exhaustion	1	4815
59 Sinusitis	1	2935
60 Hypoxia	1	2774
61 Multivariable score cut-off = 5	1	2152

Test	No. of studies	No. of participants
62 Multivariable score cut-off = 8	1	2152
63 Cough and anosmia	1	2137
64 Fever and anosmia	1	2137
65 Fever and cough and anosmia and dyspnoea and oxygen saturation < 93%	1	2137
66 Fever and dyspnoea	1	2137
67 Anosmia and dyspnoea	1	2137
68 Fever and cough	1	2137
69 Weakness or fatigue	1	1267
70 Palpitations	1	1267
71 Anxiety	1	1267
72 Respiratory distress	1	1267
73 Hyposmia or anosmia	1	809
74 Diarrhoea and nausea	1	598
75 Isolated fever	1	598
76 Myalgia and asthenia and fever	1	598
77 Cough and fever and sputum production	1	598
78 Cough and fever and sputum production and dyspnoea	1	598
79 Isolated headache	1	598
80 Dyspnoea and cough and fever and low oxygen saturation	1	598
81 Sore throat and nasal congestion and sneezing and mild fever	1	598
82 Low body temperature	1	596
83 Expectoration	1	596
84 Tachypnoea	1	510
85 Cyanosis	1	510
86 Skin lesions	1	391
87 Rhinitis or pharyngitis	1	391
88 Dizziness or syncope	1	391
89 Pulmonary auscultation: crackling unilateral	1	391

Test	No. of studies	No. of participants
90 CSBSS (cut-off = 41.7)	1	378
91 Hyposmia	1	355
92 Hypogeusia	1	355
93 Dizziness	1	319
94 Change to chronic cough	1	240
95 Dysosmia	1	139
96 Myalgia and fatigue	1	80
97 Cough (retrospective data collection)	42	65180
98 Fever (retrospective data collection)	40	75730
99 Dyspnoea (retrospective data collection)	37	37810
100 Sore throat (retrospective data collection)	30	60871
101 Headache (retrospective data collection)	26	31768
102 Diarrhoea (retrospective data collection)	25	30746
103 Myalgia (retrospective data collection)	19	18051
104 Rhinorrhoea (retrospective data collection)	17	42230
105 Chest tightness/pain (retrospective data collection)	13	36823
106 Fatigue (retrospective data collection)	13	18006
107 Anosmia (retrospective data collection)	12	11843
108 Gastrointestinal symptoms not specified (retrospective data collection)	9	29484
109 Nasal congestion (retrospective data collection)	9	16152
110 Nausea or vomiting (retrospective data collection)	9	14911
111 Abdominal pain (retrospective data collection)	9	14565
112 Vomiting (retrospective data collection)	9	12746
113 Myalgia or arthralgia (retrospective data collection)	9	9174
114 Sputum production/productive cough (retrospective data collection)	9	4755
115 Chills/shivers (retrospective data collection)	8	11340
116 Asthenia (retrospective data collection)	7	3554
117 Anosmia or ageusia (retrospective data collection)	6	33775

Test	No. of studies	No. of participants
118 Dysgeusia (retrospective data collection)	6	4094
119 Nausea (retrospective data collection)	5	6124
120 Arthralgia (retrospective data collection)	5	1324
121 Anorexia (retrospective data collection)	4	6230
122 Wheeze (retrospective data collection)	4	5667
123 Haemoptysis (retrospective data collection)	4	4749
124 Respiratory symptoms (not specified; retrospective data collection)	4	4136
125 Skin lesions (retrospective data collection)	4	3416
126 Tachycardia (retrospective data collection)	4	2739
127 Nasal symptoms (retrospective data collection)	4	1475
128 Expectoration (retrospective data collection)	4	1283
129 Ageusia (retrospective data collection)	3	3415
130 Positive auscultation findings (retrospective data collection)	3	2917
131 Tachypnea (retrospective data collection)	3	1756
132 Anosmia/dysosmia or ageusia/dysgeusia (retrospective data collection))	2	7522
133 Earache (retrospective data collection)	2	3629
134 Sneezing (retrospective data collection)	2	3467
135 Dizziness (retrospective data collection)	2	3407
136 Malaise (retrospective data collection)	2	3184
137 Fever (subjective) (retrospective data collection)	2	2787
138 Enlargement of lymph nodes (retrospective data collection)	2	2623
139 Conjunctivitis (retrospective data collection)	2	2185
140 Hypoxia (retrospective data collection)	2	2045
141 Pulmonary auscultation: rhonchi (retrospective data collection)	2	1444
142 Loss of appetite (retrospective data collection)	2	1257
143 Altered mentation/confusion (retrospective data collection)	2	983
144 Presyncope or syncope (retrospective data collection)	2	866
145 Stomach ache (retrospective data collection)	2	835

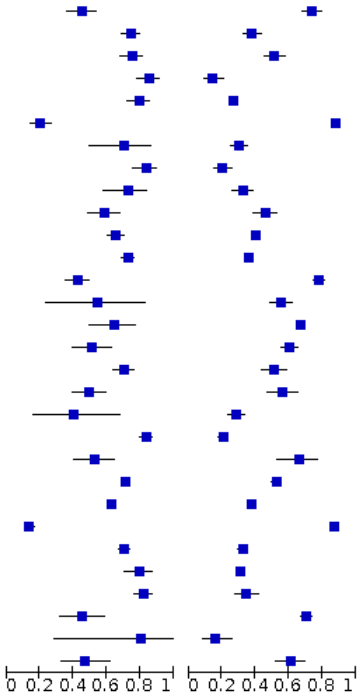
Test	No. of studies	No. of participants
146 Odynophagia (retrospective data collection)	2	793
147 Anosmia or dysgeusia (retrospective data collection)	2	686
148 Weakness or fatigue (retrospective data collection)	2	580
149 Objective fever (≥ 38 °C) or recent fever/chills (retrospective)	1	6894
150 Body aches or fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)	1	6894
151 Fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)	1	6894
152 Dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)	1	6894
153 Cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)	1	6894
154 Recent fever or chills (retrospective data collection)	1	6894
155 Sinusitis (retrospective data collection)	1	6894
156 Systemic soreness (malaise/myalgia/arthralgia) (retrospective)	1	6894
157 Malaise or fatigue (retrospective data collection)	1	3154
158 Lethargy (retrospective data collection)	1	1821
159 Nausea or vomiting or diarrhoea (retrospective data collection)	1	1747
160 Respiratory triage score > 4 (retrospective data collection)	1	1435
161 Respiratory triage score > 5 (retrospective data collection)	1	1435
162 Lower respiratory tract symptoms (retrospective data collection)	1	1210
163 Neurologic symptoms (not specified; retrospective data collection)	1	1210
164 Upper respiratory tract symptoms (retrospective data collection)	1	1210
165 Laryngitis/hoarseness/stridor (retrospective data collection)	1	1051
166 High fever (≥ 38.5 °C) (retrospective data collection)	1	1004
167 Abdominal distention (retrospective data collection)	1	936
168 Aversion to cold (retrospective data collection)	1	936
169 Xerostomia (retrospective data collection)	1	936
170 Hypersomnia (retrospective data collection)	1	936
171 Hyposmia (retrospective data collection)	1	717

Test	No. of studies	No. of participants
172 Fever and cough and dyspnoea (retrospective)	1	536
173 Fever and cough and sore throat (retrospective)	1	536
174 Fever and cough (retrospective data collection)	1	536
175 Unconsciousness (retrospective data collection)	1	475
176 Rash (retrospective data collection)	1	475
177 Fever or cough or dyspnoea (retrospective data collection)	1	404
178 Pulmonary auscultation: crackling (retrospective data collection)	1	404
179 Dysphonia (retrospective data collection)	1	253
180 Dry cough (retrospective data collection)	1	316
181 History of fever at home (retrospective data collection)	1	253
182 Cough or dyspnoea (retrospective data collection)	1	242
183 Anosmia and dysgeusia (retrospective data collection)	1	217
184 Palpitations (retrospective data collection)	1	132
185 Anosmia or hyposmia (retrospective data collection)	1	126
186 Myalgia or fatigue (retrospective data collection)	1	116
187 Respiratory distress (retrospective data collection)	1	100

Test 1. Cough

Cough

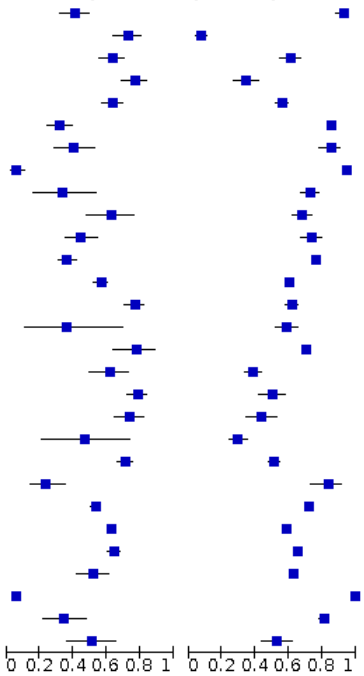
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	56	66	69	187	0.45 [0.36, 0.54]	0.74 [0.68, 0.79]
Bouzid 2020	199	203	69	125	0.74 [0.69, 0.79]	0.38 [0.33, 0.44]
Brendish 2020	128	124	42	131	0.75 [0.68, 0.82]	0.51 [0.45, 0.58]
Buonafine 2020	107	145	18	25	0.86 [0.78, 0.91]	0.15 [0.10, 0.21]
Drager 2020	129	1527	34	567	0.79 [0.72, 0.85]	0.27 [0.25, 0.29]
Ishii 2021	33	416	131	2960	0.20 [0.14, 0.27]	0.88 [0.87, 0.89]
Just 2020	19	214	8	93	0.70 [0.50, 0.86]	0.30 [0.25, 0.36]
Kalayjian 2020	98	181	19	47	0.84 [0.76, 0.90]	0.21 [0.16, 0.26]
Kempker 2020	37	157	14	75	0.73 [0.58, 0.84]	0.32 [0.26, 0.39]
Krastinova 2020	64	110	46	94	0.58 [0.48, 0.68]	0.46 [0.39, 0.53]
Maechler 2020	218	2405	115	1595	0.65 [0.60, 0.71]	0.40 [0.38, 0.41]
Mansella 2020	415	2717	157	1526	0.73 [0.69, 0.76]	0.36 [0.35, 0.37]
Nazerian 2021	82	142	111	503	0.42 [0.35, 0.50]	0.78 [0.75, 0.81]
O'Reilly 2020a	6	102	5	127	0.55 [0.23, 0.83]	0.55 [0.49, 0.62]
O'Reilly 2020b	32	421	18	863	0.64 [0.49, 0.77]	0.67 [0.65, 0.70]
Olivar Lopez 2020	39	171	37	263	0.51 [0.40, 0.63]	0.61 [0.56, 0.65]
Peyrony 2020	158	81	67	85	0.70 [0.64, 0.76]	0.51 [0.43, 0.59]
Pivetta 2020	53	53	54	68	0.50 [0.40, 0.59]	0.56 [0.47, 0.65]
Pokorska-Śpiewak 2021	6	217	9	87	0.40 [0.16, 0.68]	0.29 [0.24, 0.34]
Porto 2021	343	678	67	179	0.84 [0.80, 0.87]	0.21 [0.18, 0.24]
Romero-Gameros 2020	38	23	34	44	0.53 [0.41, 0.65]	0.66 [0.53, 0.77]
Romero-Gameros 2021	816	468	332	521	0.71 [0.68, 0.74]	0.53 [0.50, 0.56]
Rutten 2020b	917	1440	538	869	0.63 [0.60, 0.66]	0.38 [0.36, 0.40]
Saegerman 2021	78	210	495	1369	0.14 [0.11, 0.17]	0.87 [0.85, 0.88]
Salmon Ceron 2020	598	659	251	316	0.70 [0.67, 0.73]	0.32 [0.29, 0.35]
Trubiano 2020	86	1956	22	871	0.80 [0.71, 0.87]	0.31 [0.29, 0.33]
Van Loon 2021	152	122	33	64	0.82 [0.76, 0.87]	0.34 [0.28, 0.42]
Villerabel 2021	26	223	32	528	0.45 [0.32, 0.58]	0.70 [0.67, 0.74]
Wernhart 2020	4	63	1	12	0.80 [0.28, 0.99]	0.16 [0.09, 0.26]
Yonker 2020	23	49	26	76	0.47 [0.33, 0.62]	0.61 [0.52, 0.69]



Test 2. Fever

Fever

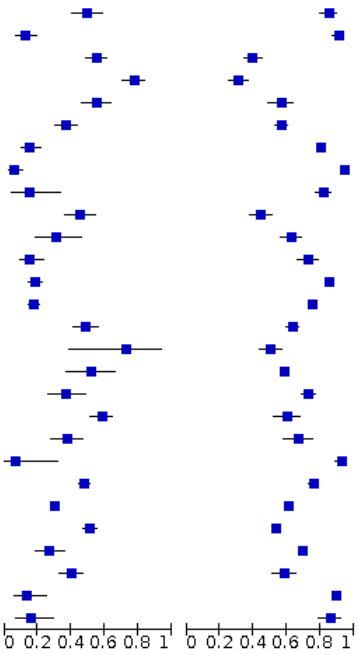
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	50	15	73	181	0.41 [0.32, 0.50]	0.92 [0.88, 0.96]
Bhattacharya 2021	91	234	34	19	0.73 [0.64, 0.80]	0.08 [0.05, 0.11]
Brendish 2020	103	97	60	152	0.63 [0.55, 0.71]	0.61 [0.55, 0.67]
Buonafine 2020	96	112	29	58	0.77 [0.68, 0.84]	0.34 [0.27, 0.42]
Clemency 2020	143	323	82	413	0.64 [0.57, 0.70]	0.56 [0.52, 0.60]
Drager 2020	52	310	111	1784	0.32 [0.25, 0.40]	0.85 [0.84, 0.87]
Fink 2021	29	22	43	125	0.40 [0.29, 0.53]	0.85 [0.78, 0.90]
Ishii 2021	10	184	154	3192	0.06 [0.03, 0.11]	0.95 [0.94, 0.95]
Just 2020	9	84	18	223	0.33 [0.17, 0.54]	0.73 [0.67, 0.78]
Kempker 2020	32	74	19	158	0.63 [0.48, 0.76]	0.68 [0.62, 0.74]
Krastinova 2020	49	54	61	150	0.45 [0.35, 0.54]	0.74 [0.67, 0.79]
Maechler 2020	121	968	212	3032	0.36 [0.31, 0.42]	0.76 [0.74, 0.77]
Mansella 2020	323	1689	249	2554	0.56 [0.52, 0.61]	0.60 [0.59, 0.62]
Nazerian 2021	148	247	45	398	0.77 [0.70, 0.82]	0.62 [0.58, 0.65]
O'Reilly 2020a	4	94	7	135	0.36 [0.11, 0.69]	0.59 [0.52, 0.65]
O'Reilly 2020b	39	383	11	901	0.78 [0.64, 0.88]	0.70 [0.68, 0.73]
Olivar Lopez 2020	47	266	29	168	0.62 [0.50, 0.73]	0.39 [0.34, 0.43]
Peyrony 2020	176	83	49	83	0.78 [0.72, 0.83]	0.50 [0.42, 0.58]
Pivetta 2020	79	68	28	53	0.74 [0.64, 0.82]	0.44 [0.35, 0.53]
Pokorska-Śpiewak 2021	7	214	8	90	0.47 [0.21, 0.73]	0.30 [0.25, 0.35]
Porto 2021	291	420	119	437	0.71 [0.66, 0.75]	0.51 [0.48, 0.54]
Romero-Gameros 2020	17	11	55	56	0.24 [0.14, 0.35]	0.84 [0.73, 0.92]
Romero-Gameros 2021	615	276	533	713	0.54 [0.51, 0.56]	0.72 [0.69, 0.75]
Rutten 2020b	917	969	538	1347	0.63 [0.60, 0.66]	0.58 [0.56, 0.60]
Saegerman 2021	368	550	205	1029	0.64 [0.60, 0.68]	0.65 [0.63, 0.68]
Trubiano 2020	56	1063	52	1764	0.52 [0.42, 0.62]	0.62 [0.61, 0.64]
Van Walraven 2021	36	71	535	8530	0.06 [0.04, 0.09]	0.99 [0.99, 0.99]
Villerabel 2021	20	142	38	609	0.34 [0.22, 0.48]	0.81 [0.78, 0.84]
Yonker 2020	25	59	24	66	0.51 [0.36, 0.66]	0.53 [0.44, 0.62]



Test 3. Dyspnoea

Dyspnoea

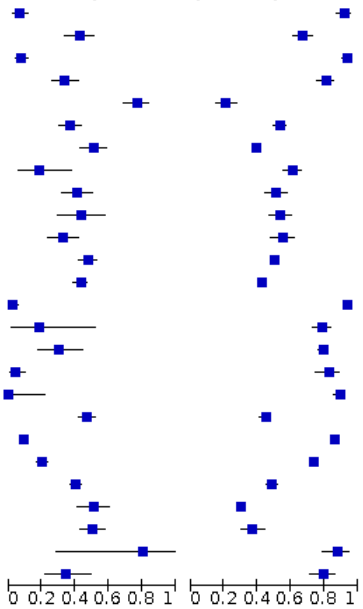
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	61	29	62	167	0.50 [0.40, 0.59]	0.85 [0.79, 0.90]
Bhattacharya 2021	16	23	109	230	0.13 [0.07, 0.20]	0.91 [0.87, 0.94]
Bouzid 2020	147	198	121	130	0.55 [0.49, 0.61]	0.40 [0.34, 0.45]
Brendish 2020	130	179	38	81	0.77 [0.70, 0.83]	0.31 [0.26, 0.37]
Buonafine 2020	69	74	56	96	0.55 [0.46, 0.64]	0.56 [0.49, 0.64]
Clemency 2020	83	318	142	418	0.37 [0.31, 0.44]	0.57 [0.53, 0.60]
Drager 2020	25	411	138	1683	0.15 [0.10, 0.22]	0.80 [0.79, 0.82]
Ishii 2021	10	176	154	3200	0.06 [0.03, 0.11]	0.95 [0.94, 0.96]
Just 2020	4	56	23	251	0.15 [0.04, 0.34]	0.82 [0.77, 0.86]
Kalayjian 2020	53	126	64	102	0.45 [0.36, 0.55]	0.45 [0.38, 0.51]
Kempker 2020	16	86	35	146	0.31 [0.19, 0.46]	0.63 [0.56, 0.69]
Krastinova 2020	17	55	93	149	0.15 [0.09, 0.24]	0.73 [0.66, 0.79]
Maechler 2020	61	597	272	3403	0.18 [0.14, 0.23]	0.85 [0.84, 0.86]
Mansella 2020	101	1057	471	3186	0.18 [0.15, 0.21]	0.75 [0.74, 0.76]
Nazerian 2021	94	237	99	408	0.49 [0.41, 0.56]	0.63 [0.59, 0.67]
O'Reilly 2020a	8	114	3	115	0.73 [0.39, 0.94]	0.50 [0.44, 0.57]
O'Reilly 2020b	26	529	24	755	0.52 [0.37, 0.66]	0.59 [0.56, 0.62]
Olivar Lopez 2020	28	117	48	317	0.37 [0.26, 0.49]	0.73 [0.69, 0.77]
Peyrony 2020	131	66	94	100	0.58 [0.51, 0.65]	0.60 [0.52, 0.68]
Pivetta 2020	40	40	67	81	0.37 [0.28, 0.47]	0.67 [0.58, 0.75]
Pokorska-Śpiewak 2021	1	23	14	281	0.07 [0.00, 0.32]	0.92 [0.89, 0.95]
Romero-Gameros 2021	550	238	598	751	0.48 [0.45, 0.51]	0.76 [0.73, 0.79]
Rutten 2020b	417	882	956	1367	0.30 [0.28, 0.33]	0.61 [0.59, 0.63]
Saegerman 2021	293	729	280	850	0.51 [0.47, 0.55]	0.54 [0.51, 0.56]
Trubiano 2020	29	868	79	1959	0.27 [0.19, 0.36]	0.69 [0.68, 0.71]
Van Loon 2021	74	77	111	109	0.40 [0.33, 0.47]	0.59 [0.51, 0.66]
Villerabel 2021	8	80	50	671	0.14 [0.06, 0.25]	0.89 [0.87, 0.91]
Yonker 2020	8	17	41	108	0.16 [0.07, 0.30]	0.86 [0.79, 0.92]



Test 4. Sore throat

Sore throat

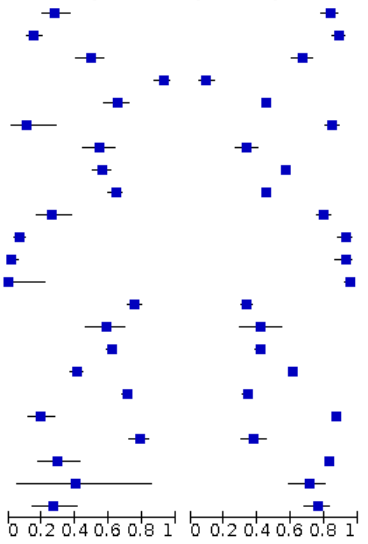
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	8	16	115	180	0.07 [0.03, 0.12]	0.92 [0.87, 0.95]
Bhattacharya 2021	53	83	72	170	0.42 [0.34, 0.52]	0.67 [0.61, 0.73]
Bouzid 2020	21	20	247	308	0.08 [0.05, 0.12]	0.94 [0.91, 0.96]
Brendish 2020	50	45	99	191	0.34 [0.26, 0.42]	0.81 [0.75, 0.86]
Buonafine 2020	96	134	29	36	0.77 [0.68, 0.84]	0.21 [0.15, 0.28]
Clemency 2020	83	344	142	392	0.37 [0.31, 0.44]	0.53 [0.50, 0.57]
Drager 2020	83	1274	80	820	0.51 [0.43, 0.59]	0.39 [0.37, 0.41]
Just 2020	5	120	22	187	0.19 [0.06, 0.38]	0.61 [0.55, 0.66]
Kalayjian 2020	48	112	69	116	0.41 [0.32, 0.50]	0.51 [0.44, 0.58]
Kempker 2020	22	108	29	124	0.43 [0.29, 0.58]	0.53 [0.47, 0.60]
Krastinova 2020	36	91	74	113	0.33 [0.24, 0.42]	0.55 [0.48, 0.62]
Maechler 2020	159	1984	174	2016	0.48 [0.42, 0.53]	0.50 [0.49, 0.52]
Mansella 2020	247	2447	325	1796	0.43 [0.39, 0.47]	0.42 [0.41, 0.44]
Nazerian 2021	6	42	187	603	0.03 [0.01, 0.07]	0.93 [0.91, 0.95]
O'Reilly 2020a	2	49	9	180	0.18 [0.02, 0.52]	0.79 [0.73, 0.84]
O'Reilly 2020b	15	270	35	1014	0.30 [0.18, 0.45]	0.79 [0.77, 0.81]
Pivetta 2020	5	21	102	100	0.05 [0.02, 0.11]	0.83 [0.75, 0.89]
Pokorska-Śpiewak 2021	0	33	15	271	0.00 [0.00, 0.22]	0.89 [0.85, 0.92]
Porto 2021	193	473	217	384	0.47 [0.42, 0.52]	0.45 [0.41, 0.48]
Rutten 2020b	94	233	882	1466	0.10 [0.08, 0.12]	0.86 [0.85, 0.88]
Saegerman 2021	117	420	456	1159	0.20 [0.17, 0.24]	0.73 [0.71, 0.76]
Salmon Ceron 2020	340	498	509	477	0.40 [0.37, 0.43]	0.49 [0.46, 0.52]
Trubiano 2020	55	1983	53	844	0.51 [0.41, 0.61]	0.30 [0.28, 0.32]
Van Loon 2021	93	117	92	69	0.50 [0.43, 0.58]	0.37 [0.30, 0.44]
Wernhart 2020	4	9	1	66	0.80 [0.28, 0.99]	0.88 [0.78, 0.94]
Yonker 2020	17	26	32	99	0.35 [0.22, 0.50]	0.79 [0.71, 0.86]



Test 5. Headache

Headache

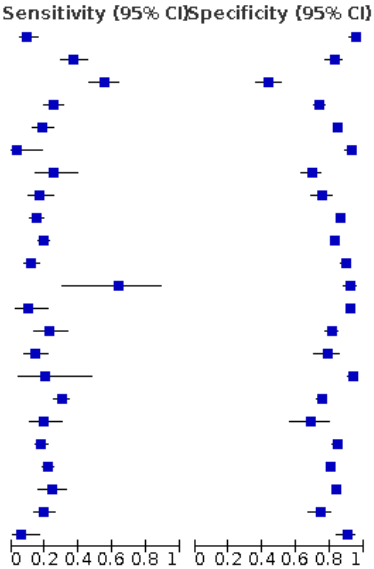
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	35	42	90	211	0.28 [0.20, 0.37]	0.83 [0.78, 0.88]
Bouzid 2020	41	37	227	291	0.15 [0.11, 0.20]	0.89 [0.85, 0.92]
Brendish 2020	73	78	76	157	0.49 [0.41, 0.57]	0.67 [0.60, 0.73]
Buonafine 2020	116	154	9	16	0.93 [0.87, 0.97]	0.09 [0.05, 0.15]
Drager 2020	106	1151	57	943	0.65 [0.57, 0.72]	0.45 [0.43, 0.47]
Just 2020	3	47	24	260	0.11 [0.02, 0.29]	0.85 [0.80, 0.89]
Krastinova 2020	60	136	50	68	0.55 [0.45, 0.64]	0.33 [0.27, 0.40]
Maechler 2020	187	1713	146	2287	0.56 [0.51, 0.62]	0.57 [0.56, 0.59]
Mansella 2020	366	2327	206	1916	0.64 [0.60, 0.68]	0.45 [0.44, 0.47]
Olivar Lopez 2020	20	88	56	346	0.26 [0.17, 0.38]	0.80 [0.76, 0.83]
Peyrony 2020	15	12	210	154	0.07 [0.04, 0.11]	0.93 [0.88, 0.96]
Pivetta 2020	2	9	105	112	0.02 [0.00, 0.07]	0.93 [0.86, 0.97]
Pokorska-Śpiewak 2021	0	15	15	289	0.00 [0.00, 0.22]	0.95 [0.92, 0.97]
Porto 2021	310	570	100	287	0.76 [0.71, 0.80]	0.33 [0.30, 0.37]
Romero-Gameros 2020	42	39	30	28	0.58 [0.46, 0.70]	0.42 [0.30, 0.54]
Romero-Gameros 2021	709	578	439	411	0.62 [0.59, 0.65]	0.42 [0.38, 0.45]
Saegerman 2021	234	614	339	965	0.41 [0.37, 0.45]	0.61 [0.59, 0.64]
Salmon Ceron 2020	603	640	246	335	0.71 [0.68, 0.74]	0.34 [0.31, 0.37]
Trubiano 2020	21	381	87	2446	0.19 [0.12, 0.28]	0.87 [0.85, 0.88]
Van Loon 2021	145	116	40	70	0.78 [0.72, 0.84]	0.38 [0.31, 0.45]
Villerabel 2021	17	128	41	623	0.29 [0.18, 0.43]	0.83 [0.80, 0.86]
Wernhart 2020	2	22	3	53	0.40 [0.05, 0.85]	0.71 [0.59, 0.81]
Yonker 2020	13	30	36	95	0.27 [0.15, 0.41]	0.76 [0.68, 0.83]



Test 6. Diarrhoea

Diarrhoea

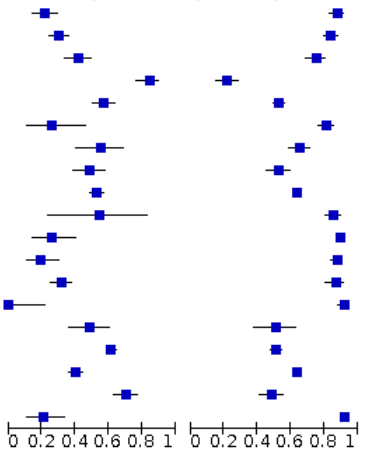
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	12	13	113	240	0.10 [0.05, 0.16]	0.95 [0.91, 0.97]
Brendish 2020	57	42	96	197	0.37 [0.30, 0.45]	0.82 [0.77, 0.87]
Buonafine 2020	69	96	56	74	0.55 [0.46, 0.64]	0.44 [0.36, 0.51]
Clemency 2020	57	192	168	544	0.25 [0.20, 0.32]	0.74 [0.71, 0.77]
Drager 2020	30	327	133	1767	0.18 [0.13, 0.25]	0.84 [0.83, 0.86]
Just 2020	1	23	26	284	0.04 [0.00, 0.19]	0.93 [0.89, 0.95]
Kempker 2020	13	72	38	160	0.25 [0.14, 0.40]	0.69 [0.63, 0.75]
Krastinova 2020	19	50	91	154	0.17 [0.11, 0.26]	0.75 [0.69, 0.81]
Maechler 2020	51	547	282	3453	0.15 [0.12, 0.20]	0.86 [0.85, 0.87]
Mansella 2020	112	730	460	3513	0.20 [0.16, 0.23]	0.83 [0.82, 0.84]
Nazerian 2021	23	70	170	575	0.12 [0.08, 0.17]	0.89 [0.86, 0.91]
O'Reilly 2020a	7	18	4	211	0.64 [0.31, 0.89]	0.92 [0.88, 0.95]
O'Reilly 2020b	5	99	45	1185	0.10 [0.03, 0.22]	0.92 [0.91, 0.94]
Olivar Lopez 2020	17	83	59	351	0.22 [0.14, 0.33]	0.81 [0.77, 0.84]
Pivetta 2020	15	26	92	95	0.14 [0.08, 0.22]	0.79 [0.70, 0.85]
Pokorska-Śpiewak 2021	3	20	12	284	0.20 [0.04, 0.48]	0.93 [0.90, 0.96]
Porto 2021	123	214	287	643	0.30 [0.26, 0.35]	0.75 [0.72, 0.78]
Romero-Gameros 2020	14	21	58	46	0.19 [0.11, 0.30]	0.69 [0.56, 0.79]
Rutten 2020b	74	139	343	730	0.18 [0.14, 0.22]	0.84 [0.81, 0.86]
Saegerman 2021	125	318	448	1261	0.22 [0.18, 0.25]	0.80 [0.78, 0.82]
Trubiano 2020	26	457	82	2370	0.24 [0.16, 0.33]	0.84 [0.82, 0.85]
Van Loon 2021	36	48	149	138	0.19 [0.14, 0.26]	0.74 [0.67, 0.80]
Yonker 2020	3	12	46	113	0.06 [0.01, 0.17]	0.90 [0.84, 0.95]



Test 7. Myalgia

Myalgia

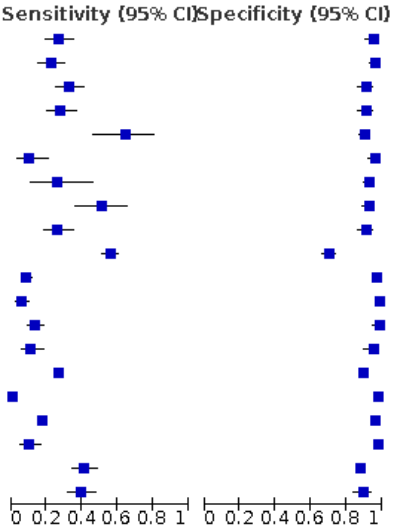
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	27	31	98	222	0.22 [0.15, 0.30]	0.88 [0.83, 0.92]
Bouzid 2020	81	53	187	275	0.30 [0.25, 0.36]	0.84 [0.79, 0.88]
Brendish 2020	62	58	87	174	0.42 [0.34, 0.50]	0.75 [0.69, 0.80]
Buonafine 2020	105	133	20	37	0.84 [0.76, 0.90]	0.22 [0.16, 0.29]
Clemency 2020	128	347	97	389	0.57 [0.50, 0.63]	0.53 [0.49, 0.57]
Just 2020	7	59	20	248	0.26 [0.11, 0.46]	0.81 [0.76, 0.85]
Kempker 2020	28	80	23	152	0.55 [0.40, 0.69]	0.66 [0.59, 0.72]
Krastinova 2020	53	97	57	107	0.48 [0.39, 0.58]	0.52 [0.45, 0.59]
Mansella 2020	301	1558	271	2685	0.53 [0.48, 0.57]	0.63 [0.62, 0.65]
O'Reilly 2020a	6	33	5	196	0.55 [0.23, 0.83]	0.86 [0.80, 0.90]
O'Reilly 2020b	13	139	37	1145	0.26 [0.15, 0.40]	0.89 [0.87, 0.91]
Olivar Lopez 2020	15	54	61	380	0.20 [0.11, 0.30]	0.88 [0.84, 0.91]
Peyrony 2020	71	22	154	144	0.32 [0.26, 0.38]	0.87 [0.81, 0.92]
Pokorska-Śpiewak 2021	0	25	15	279	0.00 [0.00, 0.22]	0.92 [0.88, 0.95]
Romero-Gameros 2020	35	33	37	34	0.49 [0.37, 0.61]	0.51 [0.38, 0.63]
Romero-Gameros 2021	705	483	443	506	0.61 [0.59, 0.64]	0.51 [0.48, 0.54]
Saegerman 2021	230	570	343	1009	0.40 [0.36, 0.44]	0.64 [0.61, 0.66]
Van Loon 2021	130	96	55	90	0.70 [0.63, 0.77]	0.48 [0.41, 0.56]
Villerabel 2021	12	58	46	693	0.21 [0.11, 0.33]	0.92 [0.90, 0.94]



Test 8. Anosmia

Anosmia

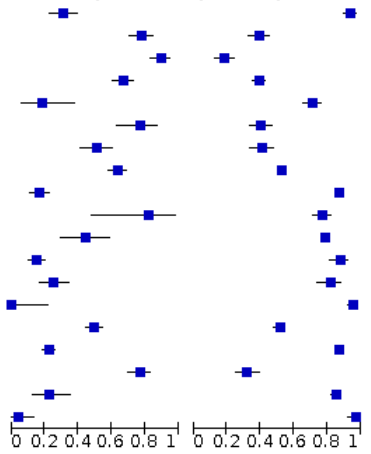
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	33	10	90	186	0.27 [0.19, 0.36]	0.95 [0.91, 0.98]
Bhattacharya 2021	28	10	97	243	0.22 [0.15, 0.31]	0.96 [0.93, 0.98]
Brendish 2020	47	19	95	197	0.33 [0.25, 0.41]	0.91 [0.87, 0.95]
Buonafine 2020	35	15	90	155	0.28 [0.20, 0.37]	0.91 [0.86, 0.95]
Haehner 2020	22	47	12	419	0.65 [0.46, 0.80]	0.90 [0.87, 0.92]
Jeyashree 2021	6	9	52	210	0.10 [0.04, 0.21]	0.96 [0.92, 0.98]
Just 2020	7	22	20	285	0.26 [0.11, 0.46]	0.93 [0.89, 0.95]
Kempker 2020	26	17	25	215	0.51 [0.37, 0.65]	0.93 [0.89, 0.96]
Krastinova 2020	29	18	81	186	0.26 [0.18, 0.36]	0.91 [0.86, 0.95]
Leal 2020	249	192	195	448	0.56 [0.51, 0.61]	0.70 [0.66, 0.74]
Maechler 2020	29	112	304	3888	0.09 [0.06, 0.12]	0.97 [0.97, 0.98]
Nazerian 2021	12	7	181	638	0.06 [0.03, 0.11]	0.99 [0.98, 1.00]
Peyrony 2020	31	3	194	163	0.14 [0.10, 0.19]	0.98 [0.95, 1.00]
Pivetta 2020	12	6	95	115	0.11 [0.06, 0.19]	0.95 [0.90, 0.98]
Romero-Gameros 2021	309	101	839	888	0.27 [0.24, 0.30]	0.90 [0.88, 0.92]
Saegerman 2021	7	35	566	1544	0.01 [0.00, 0.03]	0.98 [0.97, 0.98]
Salmon Ceron 2020	149	41	700	934	0.18 [0.15, 0.20]	0.96 [0.94, 0.97]
Trubiano 2020	11	64	97	2763	0.10 [0.05, 0.17]	0.98 [0.97, 0.98]
Tudrej 2020	82	74	116	544	0.41 [0.34, 0.49]	0.88 [0.85, 0.90]
Van Loon 2021	62	16	94	140	0.40 [0.32, 0.48]	0.90 [0.84, 0.94]



Test 9. Fatigue

Fatigue

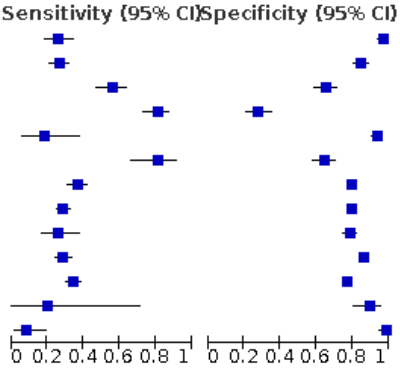
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	38	12	85	184	0.31 [0.23, 0.40]	0.94 [0.90, 0.97]
Brendish 2020	117	144	33	92	0.78 [0.71, 0.84]	0.39 [0.33, 0.46]
Buonafine 2020	112	139	13	31	0.90 [0.83, 0.94]	0.18 [0.13, 0.25]
Clemency 2020	150	447	75	289	0.67 [0.60, 0.73]	0.39 [0.36, 0.43]
Just 2020	5	89	22	218	0.19 [0.06, 0.38]	0.71 [0.66, 0.76]
Kempker 2020	39	139	12	93	0.76 [0.63, 0.87]	0.40 [0.34, 0.47]
Krastinova 2020	56	121	54	83	0.51 [0.41, 0.61]	0.41 [0.34, 0.48]
Maechler 2020	212	1888	121	2112	0.64 [0.58, 0.69]	0.53 [0.51, 0.54]
Nazerian 2021	32	82	161	563	0.17 [0.12, 0.23]	0.87 [0.84, 0.90]
O'Reilly 2020a	9	53	2	176	0.82 [0.48, 0.98]	0.77 [0.71, 0.82]
O'Reilly 2020b	22	271	28	1013	0.44 [0.30, 0.59]	0.79 [0.77, 0.81]
Peyrony 2020	34	21	191	145	0.15 [0.11, 0.20]	0.87 [0.81, 0.92]
Pivetta 2020	27	22	80	99	0.25 [0.17, 0.35]	0.82 [0.74, 0.88]
Pokorska-Śpiewak 2021	0	14	15	290	0.00 [0.00, 0.22]	0.95 [0.92, 0.97]
Porto 2021	203	415	207	442	0.50 [0.45, 0.54]	0.52 [0.48, 0.55]
Rutten 2020b	93	112	324	757	0.22 [0.18, 0.27]	0.87 [0.85, 0.89]
Van Loon 2021	142	126	43	60	0.77 [0.70, 0.83]	0.32 [0.26, 0.39]
Villerabel 2021	13	111	45	640	0.22 [0.13, 0.35]	0.85 [0.82, 0.88]
Yonker 2020	2	4	47	121	0.04 [0.00, 0.14]	0.97 [0.92, 0.99]



Test 10. Chills/shivers

Chills/shivers

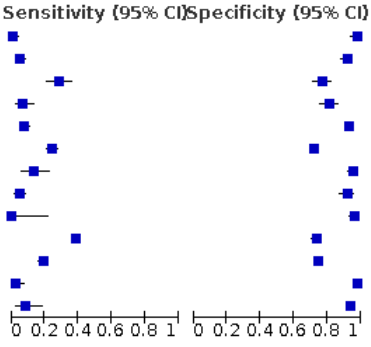
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	32	6	91	190	0.26 [0.19, 0.35]	0.97 [0.93, 0.99]
Bouzid 2020	71	50	197	278	0.26 [0.21, 0.32]	0.85 [0.80, 0.88]
Brendish 2020	84	83	67	156	0.56 [0.47, 0.64]	0.65 [0.59, 0.71]
Buonafine 2020	101	123	24	47	0.81 [0.73, 0.87]	0.28 [0.21, 0.35]
Just 2020	5	20	22	287	0.19 [0.06, 0.38]	0.93 [0.90, 0.96]
Kempker 2020	34	83	8	149	0.81 [0.66, 0.91]	0.64 [0.58, 0.70]
Maechler 2020	122	827	211	3173	0.37 [0.31, 0.42]	0.79 [0.78, 0.81]
Mansella 2020	165	860	407	3383	0.29 [0.25, 0.33]	0.80 [0.78, 0.81]
Olivar Lopez 2020	20	93	56	341	0.26 [0.17, 0.38]	0.79 [0.74, 0.82]
Porto 2021	118	121	292	736	0.29 [0.24, 0.33]	0.86 [0.83, 0.88]
Van Walraven 2021	196	1986	375	6615	0.34 [0.30, 0.38]	0.77 [0.76, 0.78]
Wernhart 2020	1	8	4	67	0.20 [0.01, 0.72]	0.89 [0.80, 0.95]
Yonker 2020	4	2	45	123	0.08 [0.02, 0.20]	0.98 [0.94, 1.00]



Test 11. Chest tightness/pain

Chest tightness/pain

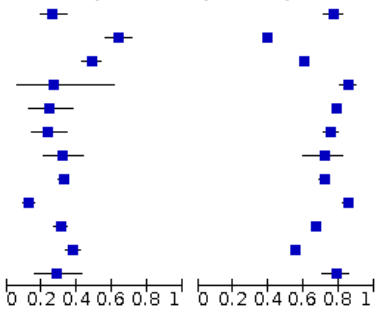
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	1	5	122	191	0.01 [0.00, 0.04]	0.97 [0.94, 0.99]
Bouzid 2020	15	28	253	300	0.06 [0.03, 0.09]	0.91 [0.88, 0.94]
Brendish 2020	43	55	107	187	0.29 [0.22, 0.37]	0.77 [0.71, 0.82]
Krastinova 2020	8	38	102	166	0.07 [0.03, 0.14]	0.81 [0.75, 0.86]
Maechler 2020	26	308	307	3692	0.08 [0.05, 0.11]	0.92 [0.91, 0.93]
Mansella 2020	139	1196	433	3047	0.24 [0.21, 0.28]	0.72 [0.70, 0.73]
Olivar Lopez 2020	10	22	66	412	0.13 [0.06, 0.23]	0.95 [0.92, 0.97]
Peyrony 2020	11	13	214	153	0.05 [0.02, 0.09]	0.92 [0.87, 0.96]
Pokorska-Śpiewak 2021	0	12	15	292	0.00 [0.00, 0.22]	0.96 [0.93, 0.98]
Romero-Gameros 2021	445	263	703	726	0.39 [0.36, 0.42]	0.73 [0.71, 0.76]
Saegerman 2021	109	401	464	1178	0.19 [0.16, 0.22]	0.75 [0.72, 0.77]
Trubiano 2020	3	68	105	2759	0.03 [0.01, 0.08]	0.98 [0.97, 0.98]
Villerabel 2021	5	47	53	704	0.09 [0.03, 0.19]	0.94 [0.92, 0.95]



Test 12. Rhinorrhea

Rhinorrhea

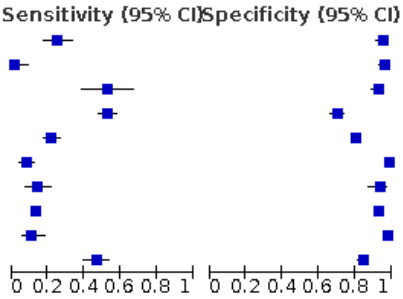
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brendish 2020	39	54	109	181	0.26 [0.19, 0.34]	0.77 [0.71, 0.82]
Drager 2020	104	1278	59	816	0.64 [0.56, 0.71]	0.39 [0.37, 0.41]
Maechler 2020	162	1594	171	2406	0.49 [0.43, 0.54]	0.60 [0.59, 0.62]
O'Reilly 2020a	3	33	8	196	0.27 [0.06, 0.61]	0.86 [0.80, 0.90]
O'Reilly 2020b	12	276	38	1008	0.24 [0.13, 0.38]	0.79 [0.76, 0.81]
Olivar Lopez 2020	18	106	58	328	0.24 [0.15, 0.35]	0.76 [0.71, 0.80]
Romero-Gameros 2020	23	19	49	48	0.32 [0.21, 0.44]	0.72 [0.59, 0.82]
Romero-Gameros 2021	373	279	775	710	0.32 [0.30, 0.35]	0.72 [0.69, 0.75]
Rutten 2020b	52	130	365	739	0.12 [0.09, 0.16]	0.85 [0.82, 0.87]
Saegerman 2021	176	521	397	1058	0.31 [0.27, 0.35]	0.67 [0.65, 0.69]
Van Walraven 2021	215	3874	356	4727	0.38 [0.34, 0.42]	0.55 [0.54, 0.56]
Yonker 2020	14	27	35	98	0.29 [0.17, 0.43]	0.78 [0.70, 0.85]



Test 13. Ageusia

Ageusia

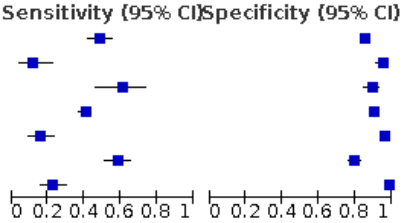
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	31	9	92	187	0.25 [0.18, 0.34]	0.95 [0.91, 0.98]
Jeyashree 2021	1	8	57	211	0.02 [0.00, 0.09]	0.96 [0.93, 0.98]
Kempker 2020	27	17	24	215	0.53 [0.38, 0.67]	0.93 [0.89, 0.96]
Leal 2020	235	192	209	448	0.53 [0.48, 0.58]	0.70 [0.66, 0.74]
Maechler 2020	73	777	260	3223	0.22 [0.18, 0.27]	0.81 [0.79, 0.82]
Nazerian 2021	16	10	177	635	0.08 [0.05, 0.13]	0.98 [0.97, 0.99]
Pivetta 2020	15	8	92	113	0.14 [0.08, 0.22]	0.93 [0.87, 0.97]
Salmon Ceron 2020	116	74	733	901	0.14 [0.11, 0.16]	0.92 [0.91, 0.94]
Trubiano 2020	12	69	96	2758	0.11 [0.06, 0.19]	0.98 [0.97, 0.98]
Tudrej 2020	92	96	106	522	0.46 [0.39, 0.54]	0.84 [0.81, 0.87]



Test 14. Anosmia or ageusia

Anosmia or ageusia

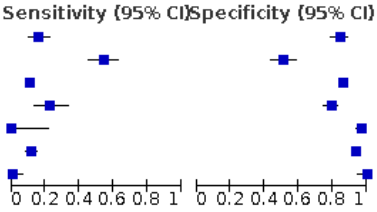
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Clemency 2020	110	108	115	628	0.49 [0.42, 0.56]	0.85 [0.83, 0.88]
Jeyashree 2021	7	11	51	208	0.12 [0.05, 0.23]	0.95 [0.91, 0.97]
Kempker 2020	31	24	20	208	0.61 [0.46, 0.74]	0.90 [0.85, 0.93]
Salmon Ceron 2020	346	95	503	880	0.41 [0.37, 0.44]	0.90 [0.88, 0.92]
Trubiano 2020	17	109	91	2718	0.16 [0.09, 0.24]	0.96 [0.95, 0.97]
Tudrej 2020	116	126	82	492	0.59 [0.51, 0.66]	0.80 [0.76, 0.83]
Wee 2020	35	9	119	707	0.23 [0.16, 0.30]	0.99 [0.98, 0.99]



Test 15. Abdominal pain

Abdominal pain

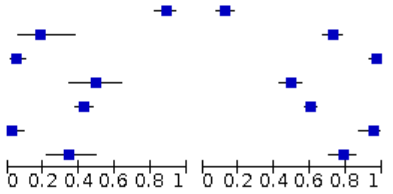
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brendish 2020	24	38	127	199	0.16 [0.10, 0.23]	0.84 [0.79, 0.88]
Buonafine 2020	68	83	57	87	0.54 [0.45, 0.63]	0.51 [0.43, 0.59]
Mansella 2020	63	601	509	3642	0.11 [0.09, 0.14]	0.86 [0.85, 0.87]
Olivar Lopez 2020	17	91	59	343	0.22 [0.14, 0.33]	0.79 [0.75, 0.83]
Pokorska-Śpiewak 2021	0	10	15	294	0.00 [0.00, 0.22]	0.97 [0.94, 0.98]
Porto 2021	49	53	361	804	0.12 [0.09, 0.15]	0.94 [0.92, 0.95]
Romero-Gameros 2020	1	0	71	67	0.01 [0.00, 0.07]	1.00 [0.95, 1.00]



Test 16. Nasal congestion

Nasal congestion

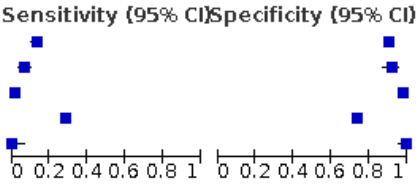
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Buonafine 2020	111	149	14	21	0.89 [0.82, 0.94]	0.12 [0.08, 0.18]
Just 2020	5	84	22	223	0.19 [0.06, 0.38]	0.73 [0.67, 0.78]
Kalayjian 2020	6	8	111	220	0.05 [0.02, 0.11]	0.96 [0.93, 0.98]
Kempker 2020	25	118	26	114	0.49 [0.35, 0.63]	0.49 [0.43, 0.56]
Porto 2021	176	341	234	516	0.43 [0.38, 0.48]	0.60 [0.57, 0.64]
Romero-Gameros 2020	2	3	70	64	0.03 [0.00, 0.10]	0.96 [0.87, 0.99]
Yonker 2020	17	27	32	98	0.35 [0.22, 0.50]	0.78 [0.70, 0.85]



Test 17. Altered mentation/confusion

Altered mentation/confusion

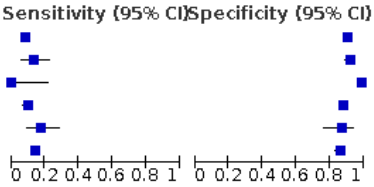
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	76	433	496	3810	0.13 [0.11, 0.16]	0.90 [0.89, 0.91]
Peyrony 2020	15	13	210	153	0.07 [0.04, 0.11]	0.92 [0.87, 0.96]
Porto 2021	7	18	403	839	0.02 [0.01, 0.03]	0.98 [0.97, 0.99]
Rutten 2020b	372	570	916	1568	0.29 [0.26, 0.31]	0.73 [0.71, 0.75]
Yonker 2020	0	1	49	124	0.00 [0.00, 0.07]	0.99 [0.96, 1.00]



Test 18. Conjunctivitis

Conjunctivitis

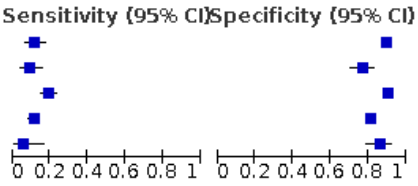
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	51	418	521	3825	0.09 [0.07, 0.12]	0.90 [0.89, 0.91]
Olivar Lopez 2020	10	35	66	399	0.13 [0.06, 0.23]	0.92 [0.89, 0.94]
Pokorska-Śpiewak 2021	0	5	15	299	0.00 [0.00, 0.22]	0.98 [0.96, 0.99]
Porto 2021	41	106	369	751	0.10 [0.07, 0.13]	0.88 [0.85, 0.90]
Romero-Gameros 2020	13	9	59	58	0.18 [0.10, 0.29]	0.87 [0.76, 0.94]
Romero-Gameros 2021	162	142	986	847	0.14 [0.12, 0.16]	0.86 [0.83, 0.88]



Test 19. Nausea or vomiting

Nausea or vomiting

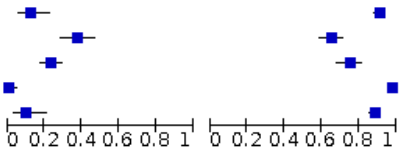
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Drager 2020	19	227	144	1867	0.12 [0.07, 0.18]	0.89 [0.88, 0.90]
Krastinova 2020	10	47	100	157	0.09 [0.04, 0.16]	0.77 [0.71, 0.83]
Porto 2021	80	86	330	771	0.20 [0.16, 0.24]	0.90 [0.88, 0.92]
Rutten 2020b	48	163	369	706	0.12 [0.09, 0.15]	0.81 [0.78, 0.84]
Yonker 2020	3	17	46	108	0.06 [0.01, 0.17]	0.86 [0.79, 0.92]



Test 20. Gastrointestinal symptoms (not specified)

Gastrointestinal symptoms (not specified)

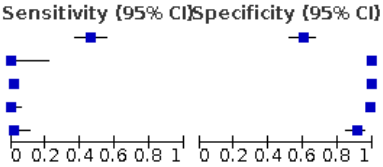
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Hüfner 2020	9	59	61	575	0.13 [0.06, 0.23]	0.91 [0.88, 0.93]		
Kalayjian 2020	44	80	73	148	0.38 [0.29, 0.47]	0.65 [0.58, 0.71]		
Peyrony 2020	53	41	172	125	0.24 [0.18, 0.30]	0.75 [0.68, 0.82]		
Trubiano 2020	1	62	107	2765	0.01 [0.00, 0.05]	0.98 [0.97, 0.98]		
Villerabel 2021	6	88	52	663	0.10 [0.04, 0.21]	0.88 [0.86, 0.90]		



Test 21. Rash

Rash

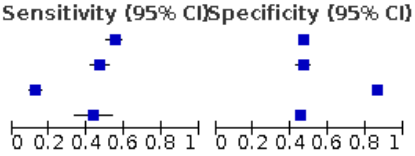
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Buonafine 2020	58	68	67	102	0.46 [0.37, 0.56]	0.60 [0.52, 0.67]		
Pokorska-Śpiewak 2021	0	1	15	303	0.00 [0.00, 0.22]	1.00 [0.98, 1.00]		
Porto 2021	7	7	403	850	0.02 [0.01, 0.03]	0.99 [0.98, 1.00]		
Villerabel 2021	0	13	58	738	0.00 [0.00, 0.06]	0.98 [0.97, 0.99]		
Yonker 2020	1	11	48	114	0.02 [0.00, 0.11]	0.91 [0.85, 0.96]		



Test 22. Coryza

Coryza

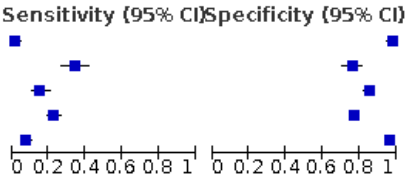
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	314	2261	258	1982	0.55 [0.51, 0.59]	0.47 [0.45, 0.48]		
Porto 2021	193	457	217	400	0.47 [0.42, 0.52]	0.47 [0.43, 0.50]		
Rutten 2020b	52	118	365	751	0.12 [0.09, 0.16]	0.86 [0.84, 0.89]		
Trubiano 2020	47	1559	61	1268	0.44 [0.34, 0.53]	0.45 [0.43, 0.47]		



Test 23. Sputum production/productive cough

Sputum production/productive cough

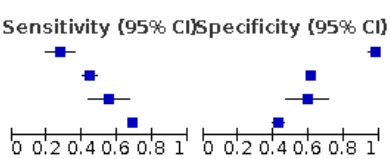
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	2	4	121	192	0.02 [0.00, 0.06]	0.98 [0.95, 0.99]		
Brendish 2020	53	56	101	181	0.34 [0.27, 0.42]	0.76 [0.70, 0.82]		
Clemency 2020	35	111	190	625	0.16 [0.11, 0.21]	0.85 [0.82, 0.87]		
Mansella 2020	132	987	440	3256	0.23 [0.20, 0.27]	0.77 [0.75, 0.78]		
Porto 2021	32	34	378	823	0.08 [0.05, 0.11]	0.96 [0.94, 0.97]		



Test 24. Asthenia

Asthenia

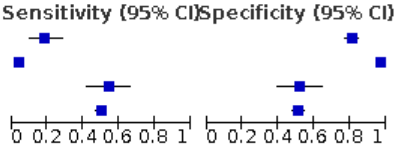
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	34	5	89	191	0.28 [0.20, 0.36]	0.97 [0.94, 0.99]		
Mansella 2020	255	1646	317	2597	0.45 [0.40, 0.49]	0.61 [0.60, 0.63]		
Romero-Gameros 2020	40	27	32	40	0.56 [0.43, 0.67]	0.60 [0.47, 0.72]		
Romero-Gameros 2021	789	565	359	424	0.69 [0.66, 0.71]	0.43 [0.40, 0.46]		



Test 25. Odynophagia

Odynophagia

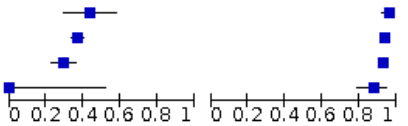
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Olivar Lopez 2020	14	82	62	352	0.18 [0.10, 0.29]	0.81 [0.77, 0.85]
Porto 2021	18	26	392	831	0.04 [0.03, 0.07]	0.97 [0.96, 0.98]
Romero-Gameros 2020	39	32	33	35	0.54 [0.42, 0.66]	0.52 [0.40, 0.65]
Romero-Gameros 2021	574	484	574	505	0.50 [0.47, 0.53]	0.51 [0.48, 0.54]



Test 26. Anosmia and ageusia

Anosmia and ageusia

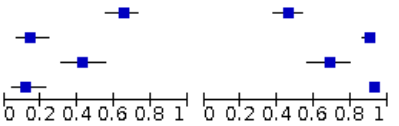
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kempker 2020	22	10	29	222	0.43 [0.29, 0.58]	0.96 [0.92, 0.98]
Salmon Ceron 2020	314	66	535	909	0.37 [0.34, 0.40]	0.93 [0.91, 0.95]
Tudrej 2020	58	44	140	574	0.29 [0.23, 0.36]	0.93 [0.91, 0.95]
Wernhart 2020	0	9	5	66	0.00 [0.00, 0.52]	0.88 [0.78, 0.94]



Test 27. Arthralgia

Arthralgia

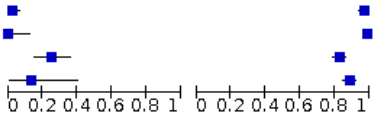
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Buonafine 2020	81	92	44	78	0.65 [0.56, 0.73]	0.46 [0.38, 0.54]
Olivar Lopez 2020	11	44	65	390	0.14 [0.07, 0.24]	0.90 [0.87, 0.93]
Romero-Gameros 2020	31	21	41	46	0.43 [0.31, 0.55]	0.69 [0.56, 0.79]
Villerabel 2021	7	57	51	694	0.12 [0.05, 0.23]	0.92 [0.90, 0.94]



Test 28. Vomiting

Vomiting

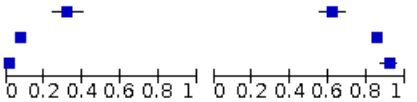
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	3	8	122	245	0.02 [0.00, 0.07]	0.97 [0.94, 0.99]
Just 2020	0	4	27	303	0.00 [0.00, 0.13]	0.99 [0.97, 1.00]
Olivar Lopez 2020	19	75	57	359	0.25 [0.16, 0.36]	0.83 [0.79, 0.86]
Pokorska-Śpiewak 2021	2	34	13	270	0.13 [0.02, 0.40]	0.89 [0.85, 0.92]



Test 29. Wheeze

Wheeze

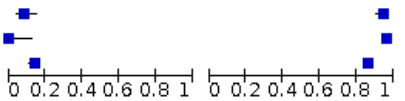
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brendish 2020	48	91	102	150	0.32 [0.25, 0.40]	0.62 [0.56, 0.68]
Mansella 2020	42	633	530	3610	0.07 [0.05, 0.10]	0.85 [0.84, 0.86]
Peyrony 2020	4	13	221	153	0.02 [0.00, 0.04]	0.92 [0.87, 0.96]



Test 30. Nausea

Nausea

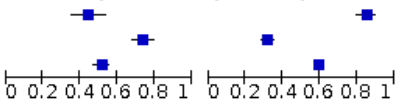
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	11	15	114	238	0.09 [0.04, 0.15]	0.94 [0.90, 0.97]		
Just 2020	0	11	27	296	0.00 [0.00, 0.13]	0.96 [0.94, 0.98]		
Mansella 2020	82	586	490	3657	0.14 [0.12, 0.17]	0.86 [0.85, 0.87]		



Test 31. Dry cough

Dry cough

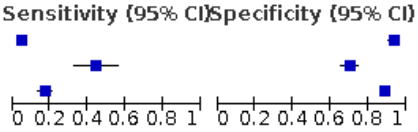
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	55	29	68	167	0.45 [0.36, 0.54]	0.85 [0.79, 0.90]		
Clemency 2020	166	500	59	236	0.74 [0.68, 0.79]	0.32 [0.29, 0.36]		
Saegerman 2021	296	639	277	940	0.52 [0.47, 0.56]	0.60 [0.57, 0.62]		



Test 32. Malaise

Malaise

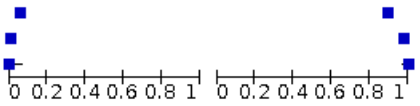
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	13	20	255	308	0.05 [0.03, 0.08]	0.94 [0.91, 0.96]		
Olivar Lopez 2020	34	130	42	304	0.45 [0.33, 0.57]	0.70 [0.65, 0.74]		
Rutten 2020b	73	101	344	768	0.18 [0.14, 0.22]	0.88 [0.86, 0.90]		



Test 33. Enlargement of lymph nodes

Enlargement of lymph nodes

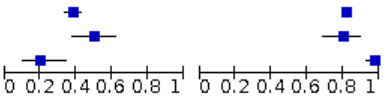
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	33	458	539	3785	0.06 [0.04, 0.08]	0.89 [0.88, 0.90]		
Porto 2021	4	21	406	836	0.01 [0.00, 0.02]	0.98 [0.96, 0.98]		
Yonker 2020	0	0	49	125	0.00 [0.00, 0.07]	1.00 [0.97, 1.00]		



Test 34. Anosmia or hyposmia

Anosmia or hyposmia

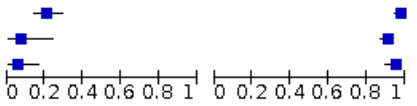
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	157	154	253	703	0.38 [0.34, 0.43]	0.82 [0.79, 0.85]		
Romero-Gameros 2020	36	13	36	54	0.50 [0.38, 0.62]	0.81 [0.69, 0.89]		
Yonker 2020	10	3	39	122	0.20 [0.10, 0.34]	0.98 [0.93, 1.00]		



Test 35. Anorexia

Anorexia

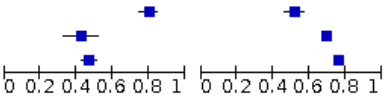
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	26	4	97	192	0.21 [0.14, 0.29]	0.98 [0.95, 0.99]		
Just 2020	2	28	25	279	0.07 [0.01, 0.24]	0.91 [0.87, 0.94]		
Yonker 2020	3	6	46	119	0.06 [0.01, 0.17]	0.95 [0.90, 0.98]		



Test 36. Fever (subjective)

Fever (subjective)

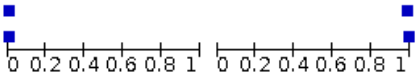
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	215	158	53	170	0.80 [0.75, 0.85]	0.52 [0.46, 0.57]		
Trubiano 2020	46	859	62	1968	0.43 [0.33, 0.52]	0.70 [0.68, 0.71]		
Van Walraven 2021	268	2089	303	6512	0.47 [0.43, 0.51]	0.76 [0.75, 0.77]		



Test 37. Haemoptysis

Haemoptysis

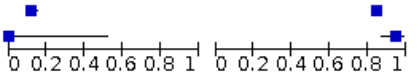
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	4	49	568	4194	0.01 [0.00, 0.02]	0.99 [0.98, 0.99]		
Peyrony 2020	3	1	222	165	0.01 [0.00, 0.04]	0.99 [0.97, 1.00]		



Test 38. Earache

Earache

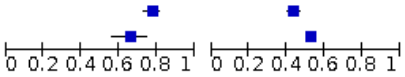
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	70	679	502	3564	0.12 [0.10, 0.15]	0.84 [0.83, 0.85]		
Wernhart 2020	0	4	5	71	0.00 [0.00, 0.52]	0.95 [0.87, 0.99]		



Test 39. Systemic soreness (malaise/myalgia/arthralgia)

Systemic soreness (malaise/myalgia/arthralgia)

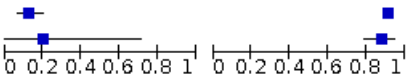
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	318	482	92	375	0.78 [0.73, 0.82]	0.44 [0.40, 0.47]		
Trubiano 2020	71	1339	37	1488	0.66 [0.56, 0.75]	0.53 [0.51, 0.54]		



Test 40. High fever (≥ 38.5 °C)

High fever (≥ 38.5 °C)

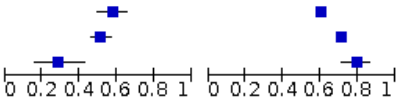
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	14	260	94	2567	0.13 [0.07, 0.21]	0.91 [0.90, 0.92]		
Wernhart 2020	1	9	4	66	0.20 [0.01, 0.72]	0.88 [0.78, 0.94]		



Test 41. Myalgia or arthralgia

Myalgia or arthralgia

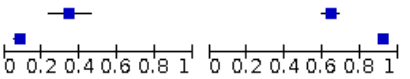
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Drager 2020	94	827	69	1267	0.58 [0.50, 0.65]	0.61 [0.58, 0.63]		
Maechler 2020	171	1145	162	2855	0.51 [0.46, 0.57]	0.71 [0.70, 0.73]		
Yonker 2020	14	26	35	99	0.29 [0.17, 0.43]	0.79 [0.71, 0.86]		



Test 42. Irritability

Irritability

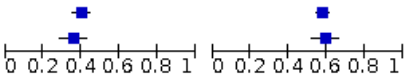
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Olivar Lopez 2020	26	154	50	280	0.34 [0.24, 0.46]	0.65 [0.60, 0.69]		
Porto 2021	34	70	376	787	0.08 [0.06, 0.11]	0.92 [0.90, 0.94]		



Test 43. Sneezing

Sneezing

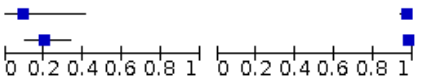
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	164	363	246	494	0.40 [0.35, 0.45]	0.58 [0.54, 0.61]		
Van Loon 2021	66	76	119	110	0.36 [0.29, 0.43]	0.59 [0.52, 0.66]		



Test 44. Anosmia or dysgeusia

Anosmia or dysgeusia

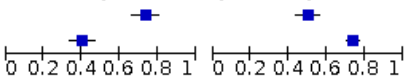
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
O'Reilly 2020a	1	7	10	222	0.09 [0.00, 0.41]	0.97 [0.94, 0.99]		
O'Reilly 2020b	10	32	40	1252	0.20 [0.10, 0.34]	0.98 [0.96, 0.98]		



Test 45. Loss of appetite

Loss of appetite

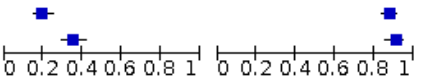
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Brendish 2020	112	116	40	116	0.74 [0.66, 0.80]	0.50 [0.43, 0.57]		
Clemency 2020	90	194	135	542	0.40 [0.34, 0.47]	0.74 [0.70, 0.77]		



Test 46. Pulmonary auscultation: crackling bilateral

Pulmonary auscultation: crackling bilateral

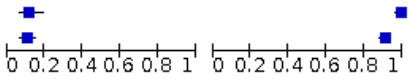
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	53	39	215	289	0.20 [0.15, 0.25]	0.88 [0.84, 0.91]		
Peyrony 2020	80	15	145	151	0.36 [0.29, 0.42]	0.91 [0.86, 0.95]		



Test 47. Sweating

Sweating

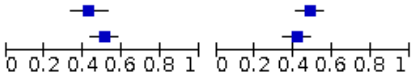
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	15	2	108	194	0.12 [0.07, 0.19]	0.99 [0.96, 1.00]		
Bouzid 2020	29	29	239	299	0.11 [0.07, 0.15]	0.91 [0.88, 0.94]		



Test 48. Nasal symptoms

Nasal symptoms

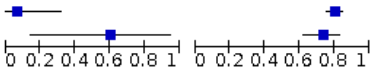
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Krastinova 2020	47	105	63	99	0.43 [0.33, 0.53]	0.49 [0.41, 0.56]		
Van Loon 2021	94	108	91	77	0.51 [0.43, 0.58]	0.42 [0.34, 0.49]		



Test 49. Rhinitis

Rhinitis

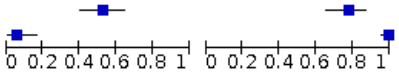
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Pokorska-Śpiewak 2021	1	59	14	245	0.07 [0.00, 0.32]	0.81 [0.76, 0.85]		
Wernhart 2020	3	20	2	55	0.60 [0.15, 0.95]	0.73 [0.62, 0.83]		



Test 50. Dysgeusia

Dysgeusia

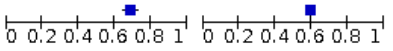
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2020	38	15	34	52	0.53 [0.41, 0.65]	0.78 [0.66, 0.87]		
Yonker 2020	3	1	46	124	0.06 [0.01, 0.17]	0.99 [0.96, 1.00]		



Test 51. SCRiPS score, recent case detection rate

SCRiPS score, recent case detection rate

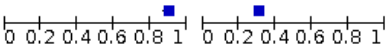
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	393	3469	178	5132	0.69 [0.65, 0.73]	0.60 [0.59, 0.61]		



Test 52. SCRIPS score, 0.5*recent case detection rate

SCRIPS score, 0.5*recent case detection rate

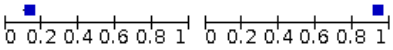
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	514	5952	57	2649	0.90 [0.87, 0.92]	0.31 [0.30, 0.32]		



Test 53. Rigors

Rigors

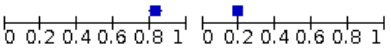
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	76	546	495	8055	0.13 [0.11, 0.16]	0.94 [0.93, 0.94]		



Test 54. Cough or dyspnoea

Cough or dyspnoea

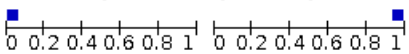
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Van Walraven 2021	473	6911	98	1690	0.83 [0.79, 0.86]	0.20 [0.19, 0.21]		



Test 55. Dysuria

Dysuria

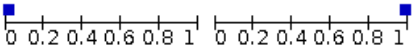
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	22	162	550	4081	0.04 [0.02, 0.06]	0.96 [0.96, 0.97]		



Test 56. Seizure

Seizure

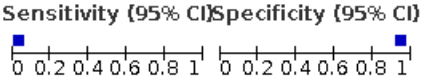
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	9	77	563	4166	0.02 [0.01, 0.03]	0.98 [0.98, 0.99]		



Test 57. Exanthema

Exanthema

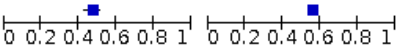
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	20	224	552	4019	0.03 [0.02, 0.05]	0.95 [0.94, 0.95]		



Test 58. Exhaustion

Exhaustion

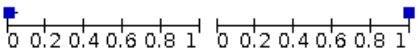
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mansella 2020	271	1860	301	2383	0.47 [0.43, 0.52]	0.56 [0.55, 0.58]		



Test 59. Sinusitis

Sinusitis

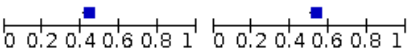
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Trubiano 2020	1	13	107	2814	0.01 [0.00, 0.05]	1.00 [0.99, 1.00]		



Test 60. Hypoxia

Hypoxia

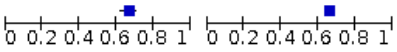
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Rutten 2020b	453	820	570	931	0.44 [0.41, 0.47]	0.53 [0.51, 0.56]		



Test 61. Multivariable score cut-off = 5

Multivariable score cut-off = 5

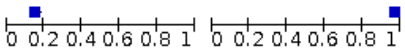
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Saegerman 2021	381	539	192	1040	0.66 [0.62, 0.70]	0.66 [0.63, 0.68]		



Test 62. Multivariable score cut-off = 8

Multivariable score cut-off = 8

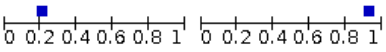
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Saegerman 2021	89	53	484	1526	0.16 [0.13, 0.19]	0.97 [0.96, 0.97]		



Test 63. Cough and anosmia

Cough and anosmia

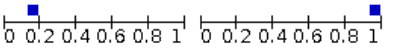
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	245	72	903	917	0.21 [0.19, 0.24]	0.93 [0.91, 0.94]		



Test 64. Fever and anosmia

Fever and anosmia

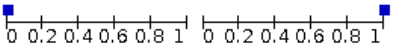
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	188	43	960	946	0.16 [0.14, 0.19]	0.96 [0.94, 0.97]		



Test 65. Fever and cough and anosmia and dyspnoea and oxygen saturation < 93%

Fever and cough and anosmia and dyspnoea and oxygen saturation < 93%

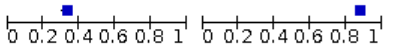
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	14	1	1134	988	0.01 [0.01, 0.02]	1.00 [0.99, 1.00]		



Test 66. Fever and dyspnoea

Fever and dyspnoea

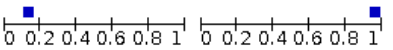
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	385	118	763	871	0.34 [0.31, 0.36]	0.88 [0.86, 0.90]		



Test 67. Anosmia and dyspnoea

Anosmia and dyspnoea

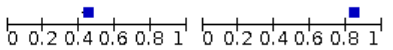
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	155	43	993	946	0.14 [0.12, 0.16]	0.96 [0.94, 0.97]		



Test 68. Fever and cough

Fever and cough

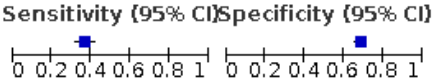
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2021	515	153	633	836	0.45 [0.42, 0.48]	0.85 [0.82, 0.87]		



Test 69. Weakness or fatigue

Weakness or fatigue

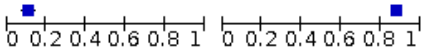
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	152	272	258	585	0.37 [0.32, 0.42]	0.68 [0.65, 0.71]		



Test 70. Palpitations

Palpitations

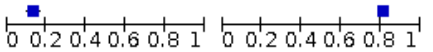
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	45	102	365	755	0.11 [0.08, 0.14]	0.88 [0.86, 0.90]		



Test 71. Anxiety

Anxiety

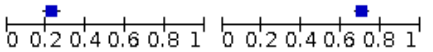
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	56	159	354	698	0.14 [0.10, 0.17]	0.81 [0.79, 0.84]		



Test 72. Respiratory distress

Respiratory distress

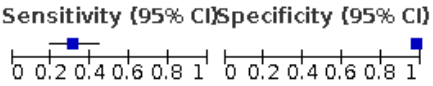
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Porto 2021	94	252	316	605	0.23 [0.19, 0.27]	0.71 [0.67, 0.74]		



Test 73. Hyposmia or anosmia

Hyposmia or anosmia

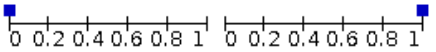
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Villerabel 2021	18	20	40	731	0.31 [0.20, 0.45]	0.97 [0.96, 0.98]		



Test 74. Diarrhoea and nausea

Diarrhoea and nausea

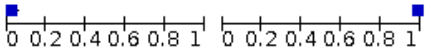
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	0	3	175	420	0.00 [0.00, 0.02]	0.99 [0.98, 1.00]		



Test 75. Isolated fever

Isolated fever

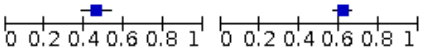
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	5	7	170	416	0.03 [0.01, 0.07]	0.98 [0.97, 0.99]		



Test 76. Myalgia and asthenia and fever

Myalgia and asthenia and fever

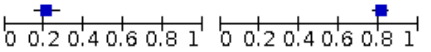
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	81	162	94	261	0.46 [0.39, 0.54]	0.62 [0.57, 0.66]		



Test 77. Cough and fever and sputum production

Cough and fever and sputum production

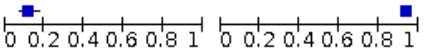
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	37	81	138	342	0.21 [0.15, 0.28]	0.81 [0.77, 0.84]		



Test 78. Cough and fever and sputum production and dyspnoea

Cough and fever and sputum production and dyspnoea

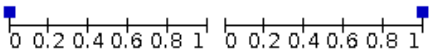
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	21	27	154	396	0.12 [0.08, 0.18]	0.94 [0.91, 0.96]		



Test 79. Isolated headache

Isolated headache

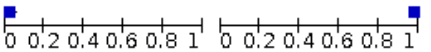
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	0	3	175	420	0.00 [0.00, 0.02]	0.99 [0.98, 1.00]		



Test 80. Dyspnoea and cough and fever and low oxygen saturation

Dyspnoea and cough and fever and low oxygen saturation

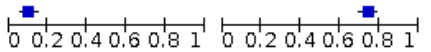
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	5	9	170	414	0.03 [0.01, 0.07]	0.98 [0.96, 0.99]		



Test 81. Sore throat and nasal congestion and sneezing and mild fever

Sore throat and nasal congestion and sneezing and mild fever

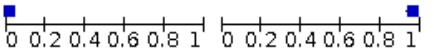
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gilbert 2020	18	109	157	314	0.10 [0.06, 0.16]	0.74 [0.70, 0.78]		



Test 82. Low body temperature

Low body temperature

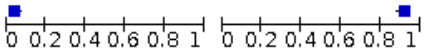
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	6	13	262	315	0.02 [0.01, 0.05]	0.96 [0.93, 0.98]		



Test 83. Expectoration

Expectoration

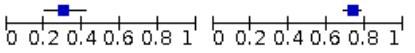
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bouzid 2020	12	27	256	301	0.04 [0.02, 0.08]	0.92 [0.88, 0.95]		



Test 84. Tachypnoea

Tachypnoea

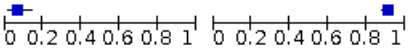
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Olivar Lopez 2020	23	115	53	319	0.30 [0.20, 0.42]	0.74 [0.69, 0.78]		



Test 85. Cyanosis

Cyanosis

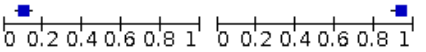
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Olivar Lopez 2020	5	40	71	394	0.07 [0.02, 0.15]	0.91 [0.88, 0.93]		



Test 86. Skin lesions

Skin lesions

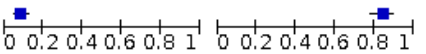
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	23	11	202	155	0.10 [0.07, 0.15]	0.93 [0.88, 0.97]		



Test 87. Rhinitis or pharyngitis

Rhinitis or pharyngitis

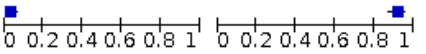
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	19	26	206	140	0.08 [0.05, 0.13]	0.84 [0.78, 0.90]		



Test 88. Dizziness or syncope

Dizziness or syncope

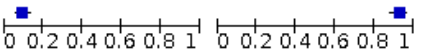
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	8	13	217	153	0.04 [0.02, 0.07]	0.92 [0.87, 0.96]		



Test 89. Pulmonary auscultation: crackling unilateral

Pulmonary auscultation: crackling unilateral

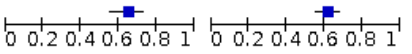
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Peyrony 2020	21	12	204	154	0.09 [0.06, 0.14]	0.93 [0.88, 0.96]		



Test 90. CSBSS (cut-off = 41.7)

CSBSS (cut-off = 41.7)

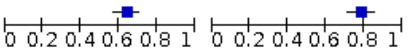
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bhattacharya 2021	81	96	44	157	0.65 [0.56, 0.73]	0.62 [0.56, 0.68]		



Test 91. Hyposmia

Hyposmia

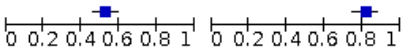
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Martin-Sanz 2020	138	30	77	110	0.64 [0.57, 0.71]	0.79 [0.71, 0.85]		



Test 92. Hypogeusia

Hypogeusia

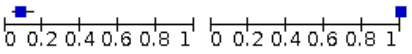
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Martin-Sanz 2020	114	25	101	115	0.53 [0.46, 0.60]	0.82 [0.75, 0.88]		



Test 93. Dizziness

Dizziness

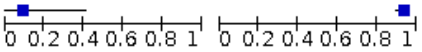
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Alizadehsani 2021	11	0	112	196	0.09 [0.05, 0.15]	1.00 [0.98, 1.00]		



Test 94. Change to chronic cough

Change to chronic cough

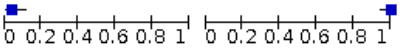
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
O'Reilly 2020a	1	14	10	215	0.09 [0.00, 0.41]	0.94 [0.90, 0.97]		



Test 95. Dysosmia

Dysosmia

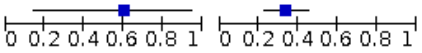
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Romero-Gameros 2020	3	0	69	67	0.04 [0.01, 0.12]	1.00 [0.95, 1.00]		



Test 96. Myalgia and fatigue

Myalgia and fatigue

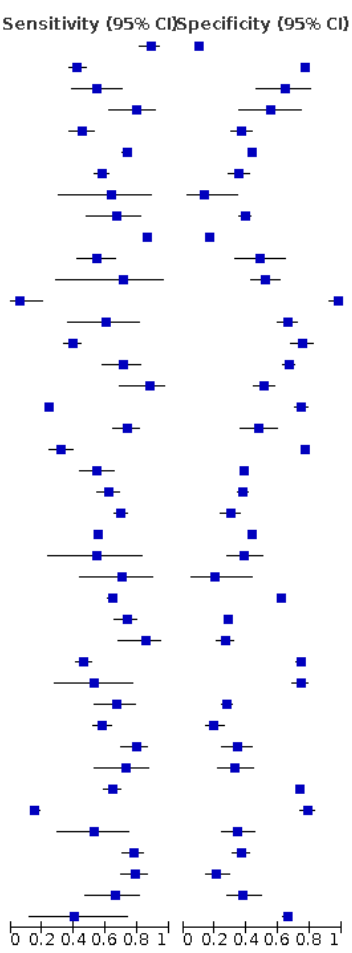
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Wernhart 2020	3	50	2	25	0.60 [0.15, 0.95]	0.33 [0.23, 0.45]		



Test 97. Cough (retrospective data collection)

Cough (retrospective data collection)

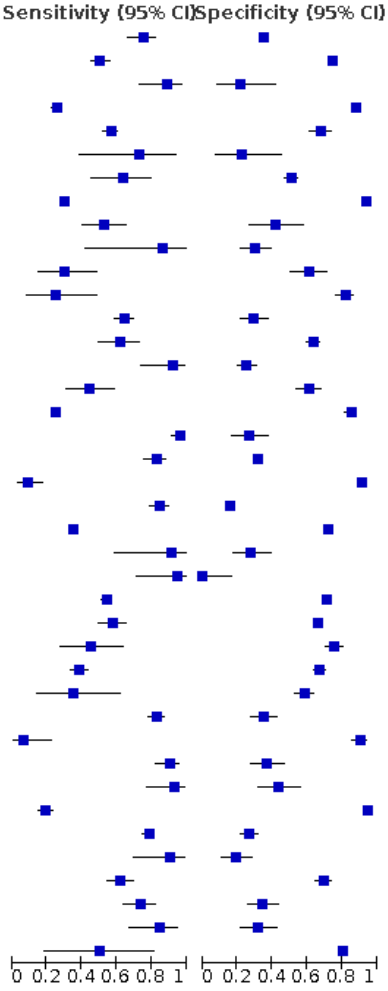
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	109	1520	14	178	0.89 [0.82, 0.94]	0.10 [0.09, 0.12]
Aldobyany 2020	143	254	197	841	0.42 [0.37, 0.48]	0.77 [0.74, 0.79]
Allegorico 2020	23	12	19	22	0.55 [0.39, 0.70]	0.65 [0.46, 0.80]
Arenas 2020	27	12	7	15	0.79 [0.62, 0.91]	0.56 [0.35, 0.75]
Arslan 2021	79	144	97	84	0.45 [0.37, 0.53]	0.37 [0.31, 0.43]
Barbhaya 2021	622	916	224	709	0.74 [0.70, 0.76]	0.44 [0.41, 0.46]
Chan 2021	293	137	217	74	0.57 [0.53, 0.62]	0.35 [0.29, 0.42]
Cheng 2020	7	19	4	3	0.64 [0.31, 0.89]	0.14 [0.03, 0.35]
Chew 2021	22	427	11	278	0.67 [0.48, 0.82]	0.39 [0.36, 0.43]
Chung 2021	788	3357	128	688	0.86 [0.84, 0.88]	0.17 [0.16, 0.18]
Cunarro-Lopez 2020	37	22	31	21	0.54 [0.42, 0.67]	0.49 [0.33, 0.65]
Feng 2021	5	60	2	65	0.71 [0.29, 0.96]	0.52 [0.43, 0.61]
Fiel-Ozores 2021	2	2	31	91	0.06 [0.01, 0.20]	0.98 [0.92, 1.00]
Haliga 2021	12	79	8	154	0.60 [0.36, 0.81]	0.66 [0.60, 0.72]
Huang 2020	132	34	204	105	0.39 [0.34, 0.45]	0.76 [0.68, 0.82]
Hüfner 2020	42	199	17	403	0.71 [0.58, 0.82]	0.67 [0.63, 0.71]
Ide 2021	22	123	3	129	0.88 [0.69, 0.97]	0.51 [0.45, 0.58]
King 2020	486	121	1501	355	0.24 [0.23, 0.26]	0.75 [0.70, 0.78]
Langer 2020	91	39	33	36	0.73 [0.65, 0.81]	0.48 [0.36, 0.60]
Lazzerini 2021	51	452	108	1537	0.32 [0.25, 0.40]	0.77 [0.75, 0.79]
Leung 2021	47	718	39	454	0.55 [0.44, 0.65]	0.39 [0.36, 0.42]
Mao 2020	116	506	72	310	0.62 [0.54, 0.69]	0.38 [0.35, 0.41]
Martín-Sánchez 2020	306	159	134	68	0.70 [0.65, 0.74]	0.30 [0.24, 0.36]
Nitecki 2021	743	12939	595	10085	0.56 [0.53, 0.58]	0.44 [0.43, 0.44]
Peng 2020	6	46	5	29	0.55 [0.23, 0.83]	0.39 [0.28, 0.51]
Pisapia 2020	12	16	5	4	0.71 [0.44, 0.90]	0.20 [0.06, 0.44]
Raberahona 2020	826	719	462	1147	0.64 [0.61, 0.67]	0.61 [0.59, 0.64]
Sacks 2020	115	1136	42	454	0.73 [0.66, 0.80]	0.29 [0.26, 0.31]
Shah 2020	28	208	5	75	0.85 [0.68, 0.95]	0.27 [0.21, 0.32]
Simpson 2020	175	213	203	619	0.46 [0.41, 0.51]	0.74 [0.71, 0.77]
Sonoda 2021	9	89	8	254	0.53 [0.28, 0.77]	0.74 [0.69, 0.79]
Sun 2020	36	528	18	206	0.67 [0.53, 0.79]	0.28 [0.25, 0.31]
Tan 2021	166	146	121	36	0.58 [0.52, 0.64]	0.20 [0.14, 0.26]
Tordjman 2020	79	66	21	34	0.79 [0.70, 0.87]	0.34 [0.25, 0.44]
Vieceli 2020	21	48	8	23	0.72 [0.53, 0.87]	0.32 [0.22, 0.45]
Vilke 2020	213	1748	117	4816	0.65 [0.59, 0.70]	0.73 [0.72, 0.74]
Wei 2020	98	65	530	243	0.16 [0.13, 0.19]	0.79 [0.74, 0.83]
Xie 2020	11	55	10	29	0.52 [0.30, 0.74]	0.35 [0.24, 0.46]
Yombi 2020	136	229	39	132	0.78 [0.71, 0.84]	0.37 [0.32, 0.42]
Zayet 2020a	75	96	20	26	0.79 [0.69, 0.87]	0.21 [0.14, 0.30]
Zhu 2020	21	52	11	32	0.66 [0.47, 0.81]	0.38 [0.28, 0.49]
Zurl 2021	4	357	6	685	0.40 [0.12, 0.74]	0.66 [0.63, 0.69]



Test 98. Fever (retrospective data collection)

Fever (retrospective data collection)

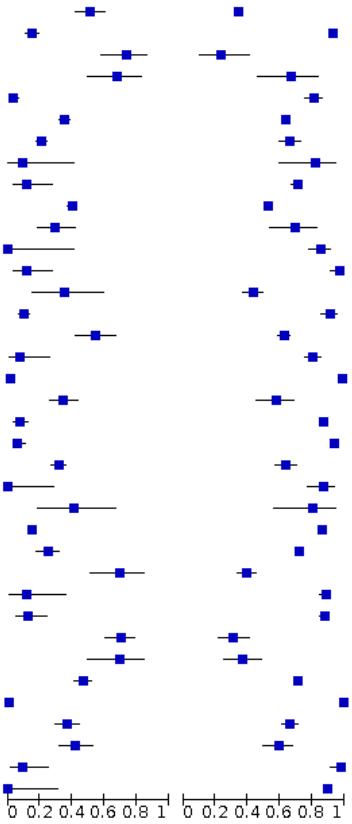
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	92	1095	31	603	0.75 [0.66, 0.82]	0.36 [0.33, 0.38]
Aldobyany 2020	172	278	168	817	0.51 [0.45, 0.56]	0.75 [0.72, 0.77]
Arenas 2020	30	21	4	6	0.88 [0.73, 0.97]	0.22 [0.09, 0.42]
Barbhaya 2021	219	206	627	1419	0.26 [0.23, 0.29]	0.87 [0.86, 0.89]
Chan 2021	288	68	222	143	0.56 [0.52, 0.61]	0.68 [0.61, 0.74]
Cheng 2020	8	17	3	5	0.73 [0.39, 0.94]	0.23 [0.08, 0.45]
Chew 2021	21	347	12	358	0.64 [0.45, 0.80]	0.51 [0.47, 0.55]
Clifford 2020	1947	702	4577	9641	0.30 [0.29, 0.31]	0.93 [0.93, 0.94]
Cunarro-Lopez 2020	36	25	32	18	0.53 [0.40, 0.65]	0.42 [0.27, 0.58]
Feng 2021	6	87	1	38	0.86 [0.42, 1.00]	0.30 [0.22, 0.39]
Fiel-Ozores 2021	10	36	23	57	0.30 [0.16, 0.49]	0.61 [0.51, 0.71]
Haliga 2021	5	43	15	190	0.25 [0.09, 0.49]	0.82 [0.76, 0.86]
Huang 2020	216	98	120	41	0.64 [0.59, 0.69]	0.29 [0.22, 0.38]
Hüfner 2020	47	230	29	397	0.62 [0.50, 0.73]	0.63 [0.59, 0.67]
Ide 2021	23	188	2	64	0.92 [0.74, 0.99]	0.25 [0.20, 0.31]
Kim 2020	24	73	30	115	0.44 [0.31, 0.59]	0.61 [0.54, 0.68]
King 2020	506	72	1481	404	0.25 [0.24, 0.27]	0.85 [0.81, 0.88]
Langer 2020	119	55	5	20	0.96 [0.91, 0.99]	0.27 [0.17, 0.38]
Lazzerini 2021	131	1355	28	634	0.82 [0.76, 0.88]	0.32 [0.30, 0.34]
Leung 2021	8	102	78	1070	0.09 [0.04, 0.18]	0.91 [0.90, 0.93]
Mao 2020	159	684	29	132	0.85 [0.79, 0.89]	0.16 [0.14, 0.19]
Nitecki 2021	470	6424	868	16600	0.35 [0.33, 0.38]	0.72 [0.72, 0.73]
Peng 2020	10	54	1	21	0.91 [0.59, 1.00]	0.28 [0.18, 0.40]
Pisapia 2020	16	20	1	0	0.94 [0.71, 1.00]	0.00 [0.00, 0.17]
Raberahona 2020	695	543	593	1323	0.54 [0.51, 0.57]	0.71 [0.69, 0.73]
Sacks 2020	90	534	67	1056	0.57 [0.49, 0.65]	0.66 [0.64, 0.69]
Shah 2020	15	69	18	214	0.45 [0.28, 0.64]	0.76 [0.70, 0.81]
Simpson 2020	147	276	231	556	0.39 [0.34, 0.44]	0.67 [0.64, 0.70]
Sonoda 2021	6	142	11	201	0.35 [0.14, 0.62]	0.59 [0.53, 0.64]
Tan 2021	237	118	50	64	0.83 [0.78, 0.87]	0.35 [0.28, 0.43]
Tolia 2020	2	25	27	227	0.07 [0.01, 0.23]	0.90 [0.86, 0.93]
Tordjman 2020	90	63	10	37	0.90 [0.82, 0.95]	0.37 [0.28, 0.47]
Vieceli 2020	27	40	2	31	0.93 [0.77, 0.99]	0.44 [0.32, 0.56]
Vilke 2020	64	368	266	6196	0.19 [0.15, 0.24]	0.94 [0.94, 0.95]
Wei 2020	491	225	137	83	0.78 [0.75, 0.81]	0.27 [0.22, 0.32]
Xie 2020	19	68	2	16	0.90 [0.70, 0.99]	0.19 [0.11, 0.29]
Yombi 2020	109	111	66	250	0.62 [0.55, 0.69]	0.69 [0.64, 0.74]
Zayet 2020a	70	80	25	42	0.74 [0.64, 0.82]	0.34 [0.26, 0.44]
Zhu 2020	27	57	5	27	0.84 [0.67, 0.95]	0.32 [0.22, 0.43]
Zurl 2021	5	205	5	851	0.50 [0.19, 0.81]	0.81 [0.78, 0.83]



Test 99. Dyspnoea (retrospective data collection)

Dyspnoea (retrospective data collection)

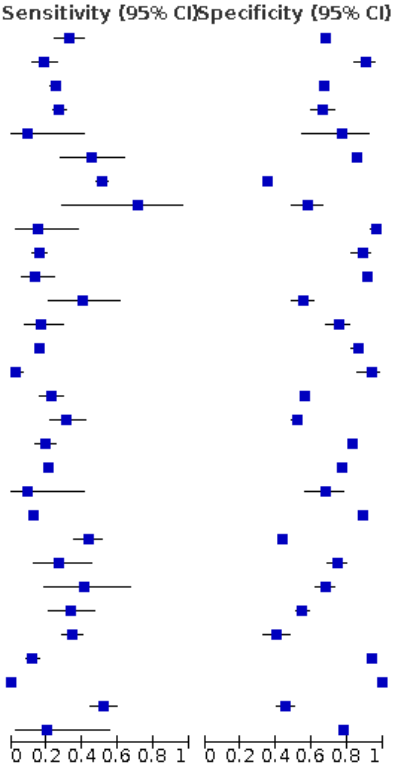
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	63	1110	60	588	0.51 [0.42, 0.60]	0.35 [0.32, 0.37]
Aldobyany 2020	51	84	289	1011	0.15 [0.11, 0.19]	0.92 [0.91, 0.94]
Allegorico 2020	31	26	11	8	0.74 [0.58, 0.86]	0.24 [0.11, 0.41]
Arenas 2020	23	9	11	18	0.68 [0.49, 0.83]	0.67 [0.46, 0.83]
Arslan 2021	6	43	170	185	0.03 [0.01, 0.07]	0.81 [0.75, 0.86]
Barbhaya 2021	297	589	549	1036	0.35 [0.32, 0.38]	0.64 [0.61, 0.66]
Chan 2021	108	71	402	140	0.21 [0.18, 0.25]	0.66 [0.60, 0.73]
Cheng 2020	1	4	10	18	0.09 [0.00, 0.41]	0.82 [0.60, 0.95]
Chew 2021	4	207	29	498	0.12 [0.03, 0.28]	0.71 [0.67, 0.74]
Chung 2021	366	1901	550	2144	0.40 [0.37, 0.43]	0.53 [0.51, 0.55]
Cunarro-Lopez 2020	20	13	48	30	0.29 [0.19, 0.42]	0.70 [0.54, 0.83]
Feng 2021	0	18	7	107	0.00 [0.00, 0.41]	0.86 [0.78, 0.91]
Fiel-Ozores 2021	4	3	29	90	0.12 [0.03, 0.28]	0.97 [0.91, 0.99]
Haliga 2021	7	132	13	101	0.35 [0.15, 0.59]	0.43 [0.37, 0.50]
Huang 2020	33	12	303	127	0.10 [0.07, 0.14]	0.91 [0.85, 0.95]
Hüfner 2020	35	236	29	397	0.55 [0.42, 0.67]	0.63 [0.59, 0.66]
Ide 2021	2	49	23	203	0.08 [0.01, 0.26]	0.81 [0.75, 0.85]
King 2020	31	6	1956	470	0.02 [0.01, 0.02]	0.99 [0.97, 1.00]
Langer 2020	43	32	81	43	0.35 [0.26, 0.44]	0.57 [0.45, 0.69]
Lazzerini 2021	12	255	147	1734	0.08 [0.04, 0.13]	0.87 [0.86, 0.89]
Mao 2020	12	51	176	765	0.06 [0.03, 0.11]	0.94 [0.92, 0.95]
Martín-Sánchez 2020	140	82	300	145	0.32 [0.27, 0.36]	0.64 [0.57, 0.70]
Peng 2020	0	10	11	65	0.00 [0.00, 0.28]	0.87 [0.77, 0.93]
Pisapia 2020	7	4	10	16	0.41 [0.18, 0.67]	0.80 [0.56, 0.94]
Raberahona 2020	199	257	1089	1609	0.15 [0.14, 0.18]	0.86 [0.85, 0.88]
Sacks 2020	39	444	118	1146	0.25 [0.18, 0.32]	0.72 [0.70, 0.74]
Shah 2020	23	171	10	112	0.70 [0.51, 0.84]	0.40 [0.34, 0.46]
Sonoda 2021	2	40	15	303	0.12 [0.01, 0.36]	0.88 [0.84, 0.92]
Sun 2020	7	93	47	641	0.13 [0.05, 0.25]	0.87 [0.85, 0.90]
Tordjman 2020	70	69	30	31	0.70 [0.60, 0.79]	0.31 [0.22, 0.41]
Vieceli 2020	20	45	9	26	0.69 [0.49, 0.85]	0.37 [0.25, 0.49]
Vilke 2020	154	1890	176	4674	0.47 [0.41, 0.52]	0.71 [0.70, 0.72]
Wei 2020	6	2	622	306	0.01 [0.00, 0.02]	0.99 [0.98, 1.00]
Yombi 2020	65	122	110	239	0.37 [0.30, 0.45]	0.66 [0.61, 0.71]
Zayet 2020a	40	50	55	72	0.42 [0.32, 0.53]	0.59 [0.50, 0.68]
Zhu 2020	3	2	29	82	0.09 [0.02, 0.25]	0.98 [0.92, 1.00]
Zurl 2021	0	113	10	927	0.00 [0.00, 0.31]	0.89 [0.87, 0.91]



Test TST-100. Sore throat (retrospective data collection)

Sore throat (retrospective data collection)

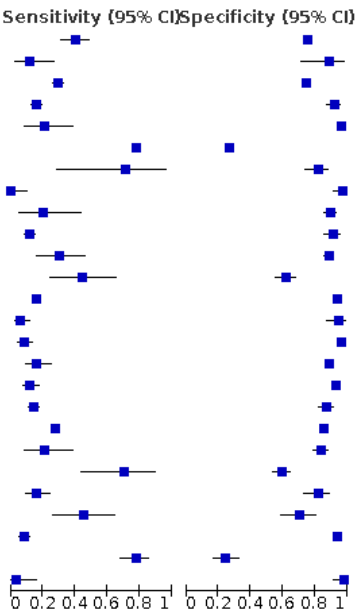
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	40	545	83	1153	0.33 [0.24, 0.42]	0.68 [0.66, 0.70]
Arslan 2021	25	11	110	103	0.19 [0.12, 0.26]	0.90 [0.83, 0.95]
Barbhaya 2021	210	532	636	1093	0.25 [0.22, 0.28]	0.67 [0.65, 0.70]
Chan 2021	139	71	371	140	0.27 [0.23, 0.31]	0.66 [0.60, 0.73]
Cheng 2020	1	5	10	17	0.09 [0.00, 0.41]	0.77 [0.55, 0.92]
Chew 2021	15	103	18	602	0.45 [0.28, 0.64]	0.85 [0.83, 0.88]
Chung 2021	467	2629	449	1416	0.51 [0.48, 0.54]	0.35 [0.34, 0.36]
Feng 2021	5	53	2	72	0.71 [0.29, 0.96]	0.58 [0.48, 0.66]
Haliga 2021	3	9	17	224	0.15 [0.03, 0.38]	0.96 [0.93, 0.98]
Huang 2020	54	16	282	123	0.16 [0.12, 0.20]	0.88 [0.82, 0.93]
Hüfner 2020	9	60	56	610	0.14 [0.07, 0.25]	0.91 [0.89, 0.93]
Ide 2021	10	113	15	139	0.40 [0.21, 0.61]	0.55 [0.49, 0.61]
Kim 2020	9	47	45	141	0.17 [0.08, 0.29]	0.75 [0.68, 0.81]
King 2020	311	67	1676	409	0.16 [0.14, 0.17]	0.86 [0.82, 0.89]
Langer 2020	3	5	121	70	0.02 [0.01, 0.07]	0.93 [0.85, 0.98]
Lazzerini 2021	36	881	123	1108	0.23 [0.16, 0.30]	0.56 [0.53, 0.58]
Leung 2021	27	563	59	609	0.31 [0.22, 0.42]	0.52 [0.49, 0.55]
Mao 2020	36	140	152	676	0.19 [0.14, 0.26]	0.83 [0.80, 0.85]
Nitecki 2021	284	5272	1054	17752	0.21 [0.19, 0.24]	0.77 [0.77, 0.78]
Peng 2020	1	24	10	51	0.09 [0.00, 0.41]	0.68 [0.56, 0.78]
Raberahona 2020	162	215	1126	1651	0.13 [0.11, 0.15]	0.88 [0.87, 0.90]
Sacks 2020	68	897	89	693	0.43 [0.35, 0.51]	0.44 [0.41, 0.46]
Shah 2020	9	73	24	210	0.27 [0.13, 0.46]	0.74 [0.69, 0.79]
Sonoda 2021	7	111	10	232	0.41 [0.18, 0.67]	0.68 [0.62, 0.73]
Sun 2020	18	332	36	402	0.33 [0.21, 0.47]	0.55 [0.51, 0.58]
Tan 2021	99	109	188	73	0.34 [0.29, 0.40]	0.40 [0.33, 0.48]
Vilke 2020	40	438	290	6126	0.12 [0.09, 0.16]	0.93 [0.93, 0.94]
Wei 2020	1	3	627	305	0.00 [0.00, 0.01]	0.99 [0.97, 1.00]
Yombi 2020	91	197	84	164	0.52 [0.44, 0.60]	0.45 [0.40, 0.51]
Zurl 2021	2	227	8	806	0.20 [0.03, 0.56]	0.78 [0.75, 0.81]



Test TST-101. Headache (retrospective data collection)

Headache (retrospective data collection)

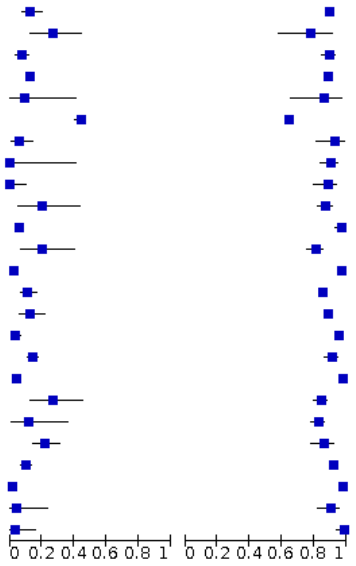
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	49	428	74	1270	0.40 [0.31, 0.49]	0.75 [0.73, 0.77]
Arenas 2020	4	3	30	24	0.12 [0.03, 0.27]	0.89 [0.71, 0.98]
Barbhaya 2021	249	416	597	1209	0.29 [0.26, 0.33]	0.74 [0.72, 0.77]
Chan 2021	82	17	428	194	0.16 [0.13, 0.20]	0.92 [0.87, 0.95]
Chew 2021	7	25	26	680	0.21 [0.09, 0.39]	0.96 [0.95, 0.98]
Chung 2021	714	2953	202	1092	0.78 [0.75, 0.81]	0.27 [0.26, 0.28]
Feng 2021	5	23	2	102	0.71 [0.29, 0.96]	0.82 [0.74, 0.88]
Fiel-Ozores 2021	0	3	33	90	0.00 [0.00, 0.11]	0.97 [0.91, 0.99]
Haliga 2021	4	24	16	209	0.20 [0.06, 0.44]	0.90 [0.85, 0.93]
Huang 2020	39	12	297	127	0.12 [0.08, 0.16]	0.91 [0.85, 0.95]
Hüfner 2020	12	69	28	527	0.30 [0.17, 0.47]	0.88 [0.86, 0.91]
Ide 2021	11	96	14	156	0.44 [0.24, 0.65]	0.62 [0.56, 0.68]
King 2020	312	30	1675	446	0.16 [0.14, 0.17]	0.94 [0.91, 0.96]
Langer 2020	8	4	116	71	0.06 [0.03, 0.12]	0.95 [0.87, 0.99]
Lazzerini 2021	13	79	146	1910	0.08 [0.04, 0.14]	0.96 [0.95, 0.97]
Leung 2021	14	131	72	1041	0.16 [0.09, 0.26]	0.89 [0.87, 0.91]
Mao 2020	23	61	165	755	0.12 [0.08, 0.18]	0.93 [0.91, 0.94]
Martín-Sánchez 2020	63	30	377	197	0.14 [0.11, 0.18]	0.87 [0.82, 0.91]
Raberahona 2020	358	276	930	1590	0.28 [0.25, 0.30]	0.85 [0.84, 0.87]
Shah 2020	7	47	26	236	0.21 [0.09, 0.39]	0.83 [0.79, 0.88]
Sonoda 2021	12	140	5	203	0.71 [0.44, 0.90]	0.59 [0.54, 0.64]
Tordjman 2020	16	18	84	82	0.16 [0.09, 0.25]	0.82 [0.73, 0.89]
Vieceli 2020	13	21	16	50	0.45 [0.26, 0.64]	0.70 [0.58, 0.81]
Vilke 2020	27	434	303	6130	0.08 [0.05, 0.12]	0.93 [0.93, 0.94]
Zayet 2020a	74	92	21	30	0.78 [0.68, 0.86]	0.25 [0.17, 0.33]
Zhu 2020	1	2	31	82	0.03 [0.00, 0.16]	0.98 [0.92, 1.00]



Test TST-102. Diarrhoea (retrospective data collection)

Diarrhoea (retrospective data collection)

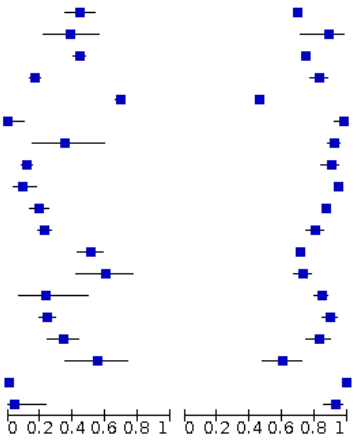
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	16	175	107	1523	0.13 [0.08, 0.20]	0.90 [0.88, 0.91]
Arenas 2020	9	6	25	21	0.26 [0.13, 0.44]	0.78 [0.58, 0.91]
Arslan 2021	13	25	163	203	0.07 [0.04, 0.12]	0.89 [0.84, 0.93]
Barbhaya 2021	106	182	740	1443	0.13 [0.10, 0.15]	0.89 [0.87, 0.90]
Cheng 2020	1	3	10	19	0.09 [0.00, 0.41]	0.86 [0.65, 0.97]
Chung 2021	403	1456	513	2589	0.44 [0.41, 0.47]	0.64 [0.63, 0.65]
Cunarro-Lopez 2020	4	3	64	40	0.06 [0.02, 0.14]	0.93 [0.81, 0.99]
Feng 2021	0	12	7	113	0.00 [0.00, 0.41]	0.90 [0.84, 0.95]
Fiel-Ozores 2021	0	11	33	82	0.00 [0.00, 0.11]	0.88 [0.80, 0.94]
Haliga 2021	4	30	16	203	0.20 [0.06, 0.44]	0.87 [0.82, 0.91]
Huang 2020	19	4	317	135	0.06 [0.03, 0.09]	0.97 [0.93, 0.99]
Ide 2021	5	48	20	204	0.20 [0.07, 0.41]	0.81 [0.76, 0.86]
King 2020	57	13	1930	463	0.03 [0.02, 0.04]	0.97 [0.95, 0.99]
Lazzerini 2021	18	293	141	1696	0.11 [0.07, 0.17]	0.85 [0.84, 0.87]
Leung 2021	11	136	75	1036	0.13 [0.07, 0.22]	0.88 [0.86, 0.90]
Mao 2020	6	37	182	779	0.03 [0.01, 0.07]	0.95 [0.94, 0.97]
Martín-Sánchez 2020	62	21	378	206	0.14 [0.11, 0.18]	0.91 [0.86, 0.94]
Raberahona 2020	61	49	1227	1817	0.05 [0.04, 0.06]	0.97 [0.97, 0.98]
Shah 2020	9	45	24	238	0.27 [0.13, 0.46]	0.84 [0.79, 0.88]
Sonoda 2021	2	60	15	283	0.12 [0.01, 0.36]	0.83 [0.78, 0.86]
Tordjman 2020	22	14	78	86	0.22 [0.14, 0.31]	0.86 [0.78, 0.92]
Vilke 2020	34	558	296	6006	0.10 [0.07, 0.14]	0.91 [0.91, 0.92]
Wei 2020	12	6	616	302	0.02 [0.01, 0.03]	0.98 [0.96, 0.99]
Xie 2020	1	8	20	76	0.05 [0.00, 0.24]	0.90 [0.82, 0.96]
Zhu 2020	1	1	31	83	0.03 [0.00, 0.16]	0.99 [0.94, 1.00]



Test TST-103. Myalgia (retrospective data collection)

Myalgia (retrospective data collection)

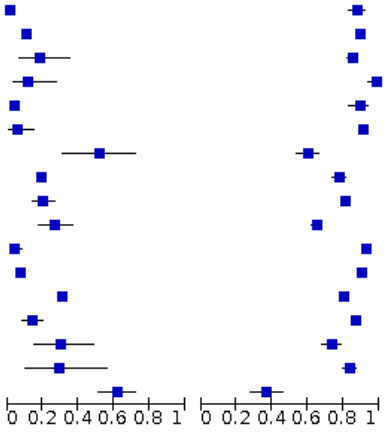
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	55	526	68	1172	0.45 [0.36, 0.54]	0.69 [0.67, 0.71]
Arenas 2020	13	3	21	24	0.38 [0.22, 0.56]	0.89 [0.71, 0.98]
Barbhaya 2021	374	417	472	1208	0.44 [0.41, 0.48]	0.74 [0.72, 0.76]
Chan 2021	87	36	423	175	0.17 [0.14, 0.21]	0.83 [0.77, 0.88]
Chung 2021	632	2184	284	1861	0.69 [0.66, 0.72]	0.46 [0.44, 0.48]
Fiel-Ozores 2021	0	2	33	91	0.00 [0.00, 0.11]	0.98 [0.92, 1.00]
Haliga 2021	7	19	13	214	0.35 [0.15, 0.59]	0.92 [0.88, 0.95]
Huang 2020	39	14	297	125	0.12 [0.08, 0.16]	0.90 [0.84, 0.94]
Leung 2021	8	69	78	1103	0.09 [0.04, 0.18]	0.94 [0.93, 0.95]
Mao 2020	36	105	152	711	0.19 [0.14, 0.26]	0.87 [0.85, 0.89]
Martín-Sánchez 2020	99	44	341	183	0.23 [0.19, 0.27]	0.81 [0.75, 0.86]
Sacks 2020	80	459	77	1131	0.51 [0.43, 0.59]	0.71 [0.69, 0.73]
Shah 2020	20	77	13	206	0.61 [0.42, 0.77]	0.73 [0.67, 0.78]
Sonoda 2021	4	54	13	289	0.24 [0.07, 0.50]	0.84 [0.80, 0.88]
Tan 2021	69	19	218	163	0.24 [0.19, 0.29]	0.90 [0.84, 0.94]
Tordjman 2020	34	17	66	83	0.34 [0.25, 0.44]	0.83 [0.74, 0.90]
Vieceli 2020	16	28	13	43	0.55 [0.36, 0.74]	0.61 [0.48, 0.72]
Wei 2020	8	2	620	306	0.01 [0.01, 0.02]	0.99 [0.98, 1.00]
Xie 2020	1	6	20	78	0.05 [0.00, 0.24]	0.93 [0.85, 0.97]



Test TST-104. Rhinorrhoea (retrospective data collection)

Rhinorrhoea (retrospective data collection)

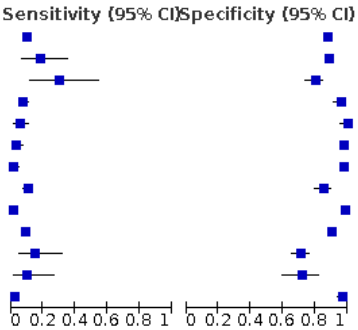
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	3	28	173	200	0.02 [0.00, 0.05]	0.88 [0.83, 0.92]
Barbhaya 2021	92	166	754	1459	0.11 [0.09, 0.13]	0.90 [0.88, 0.91]
Chew 2021	6	106	27	599	0.18 [0.07, 0.35]	0.85 [0.82, 0.88]
Fiel-Ozores 2021	4	1	29	92	0.12 [0.03, 0.28]	0.99 [0.94, 1.00]
Huang 2020	14	15	322	124	0.04 [0.02, 0.07]	0.89 [0.83, 0.94]
Hüfner 2020	3	58	50	599	0.06 [0.01, 0.16]	0.91 [0.89, 0.93]
Ide 2021	13	100	12	152	0.52 [0.31, 0.72]	0.60 [0.54, 0.66]
King 2020	383	105	1604	371	0.19 [0.18, 0.21]	0.78 [0.74, 0.82]
Lazzerini 2021	32	372	127	1617	0.20 [0.14, 0.27]	0.81 [0.80, 0.83]
Leung 2021	23	412	63	760	0.27 [0.18, 0.37]	0.65 [0.62, 0.68]
Mao 2020	9	59	179	757	0.05 [0.02, 0.09]	0.93 [0.91, 0.94]
Nitecki 2021	106	2192	1232	20832	0.08 [0.07, 0.10]	0.90 [0.90, 0.91]
Raberahona 2020	400	377	888	1489	0.31 [0.29, 0.34]	0.80 [0.78, 0.82]
Sacks 2020	22	204	135	1386	0.14 [0.09, 0.20]	0.87 [0.85, 0.89]
Shah 2020	10	74	23	209	0.30 [0.16, 0.49]	0.74 [0.68, 0.79]
Sonoda 2021	5	56	12	287	0.29 [0.10, 0.56]	0.84 [0.79, 0.87]
Zayet 2020a	59	77	36	45	0.62 [0.52, 0.72]	0.37 [0.28, 0.46]



Test TST-105. Chest tightness/pain (retrospective data collection)

Chest tightness/pain (retrospective data collection)

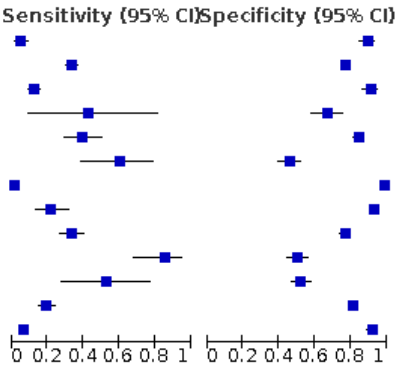
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	89	193	757	1432	0.11 [0.09, 0.13]	0.88 [0.86, 0.90]
Chew 2021	6	81	27	624	0.18 [0.07, 0.35]	0.89 [0.86, 0.91]
Haliga 2021	6	47	14	186	0.30 [0.12, 0.54]	0.80 [0.74, 0.85]
Huang 2020	27	6	309	133	0.08 [0.05, 0.11]	0.96 [0.91, 0.98]
Langer 2020	7	0	117	75	0.06 [0.02, 0.11]	1.00 [0.95, 1.00]
Lazzerini 2021	6	44	153	1945	0.04 [0.01, 0.08]	0.98 [0.97, 0.98]
Mao 2020	4	19	184	797	0.02 [0.01, 0.05]	0.98 [0.96, 0.99]
Martín-Sánchez 2020	47	34	393	193	0.11 [0.08, 0.14]	0.85 [0.80, 0.89]
Nitecki 2021	24	406	1314	22618	0.02 [0.01, 0.03]	0.98 [0.98, 0.98]
Raberahona 2020	118	178	1170	1688	0.09 [0.08, 0.11]	0.90 [0.89, 0.92]
Shah 2020	5	81	28	202	0.15 [0.05, 0.32]	0.71 [0.66, 0.77]
Vieceli 2020	3	20	26	51	0.10 [0.02, 0.27]	0.72 [0.60, 0.82]
Wei 2020	15	10	613	298	0.02 [0.01, 0.04]	0.97 [0.94, 0.98]



Test TST-106. Fatigue (retrospective data collection)

Fatigue (retrospective data collection)

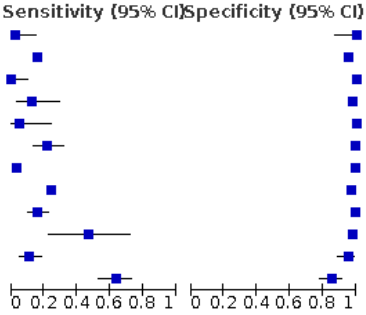
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	9	24	167	204	0.05 [0.02, 0.09]	0.89 [0.85, 0.93]
Barbhaya 2021	286	377	560	1248	0.34 [0.31, 0.37]	0.77 [0.75, 0.79]
Chan 2021	65	19	445	192	0.13 [0.10, 0.16]	0.91 [0.86, 0.94]
Feng 2021	3	41	4	84	0.43 [0.10, 0.82]	0.67 [0.58, 0.75]
Hüfner 2020	36	106	55	573	0.40 [0.29, 0.50]	0.84 [0.81, 0.87]
Ide 2021	15	137	10	115	0.60 [0.39, 0.79]	0.46 [0.39, 0.52]
King 2020	31	6	1956	470	0.02 [0.01, 0.02]	0.99 [0.97, 1.00]
Leung 2021	19	87	67	1085	0.22 [0.14, 0.32]	0.93 [0.91, 0.94]
Mao 2020	63	187	125	629	0.34 [0.27, 0.41]	0.77 [0.74, 0.80]
Shah 2020	28	140	5	143	0.85 [0.68, 0.95]	0.51 [0.45, 0.56]
Sonoda 2021	9	164	8	179	0.53 [0.28, 0.77]	0.52 [0.47, 0.58]
Vilke 2020	65	1254	265	5310	0.20 [0.16, 0.24]	0.81 [0.80, 0.82]
Wei 2020	42	24	586	284	0.07 [0.05, 0.09]	0.92 [0.89, 0.95]



Test TST-107. Anosmia (retrospective data collection)

Anosmia (retrospective data collection)

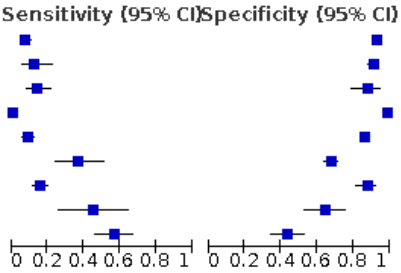
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arenas 2020	1	0	33	27	0.03 [0.00, 0.15]	1.00 [0.87, 1.00]
Barbhaya 2021	139	79	707	1546	0.16 [0.14, 0.19]	0.95 [0.94, 0.96]
Chew 2021	0	1	33	704	0.00 [0.00, 0.11]	1.00 [0.99, 1.00]
Chua 2020	4	14	27	672	0.13 [0.04, 0.30]	0.98 [0.97, 0.99]
Haliga 2021	1	0	19	233	0.05 [0.00, 0.25]	1.00 [0.98, 1.00]
Leung 2021	19	3	67	1169	0.22 [0.14, 0.32]	1.00 [0.99, 1.00]
Martín-Sánchez 2020	14	2	426	225	0.03 [0.02, 0.05]	0.99 [0.97, 1.00]
Raberahona 2020	311	63	977	1803	0.24 [0.22, 0.27]	0.97 [0.96, 0.97]
Sacks 2020	25	15	132	1575	0.16 [0.11, 0.23]	0.99 [0.98, 0.99]
Sonoda 2021	8	9	9	334	0.47 [0.23, 0.72]	0.97 [0.95, 0.99]
Tordjman 2020	11	5	89	95	0.11 [0.06, 0.19]	0.95 [0.89, 0.98]
Zayet 2020a	60	18	35	104	0.63 [0.53, 0.73]	0.85 [0.78, 0.91]



Test TST-108. Gastrointestinal symptoms not specified (retrospective data collection)

Gastrointestinal symptoms not specified (retrospective data collection)

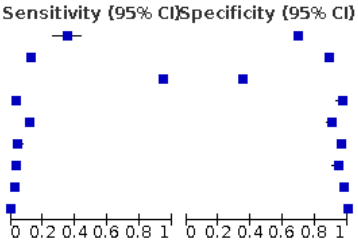
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aldobyany 2020	26	84	314	1011	0.08 [0.05, 0.11]	0.92 [0.91, 0.94]
Hüfner 2020	9	59	61	575	0.13 [0.06, 0.23]	0.91 [0.88, 0.93]
Langer 2020	18	9	106	66	0.15 [0.09, 0.22]	0.88 [0.78, 0.94]
Nitecki 2021	17	322	1321	22702	0.01 [0.01, 0.02]	0.99 [0.98, 0.99]
Simpson 2020	35	115	343	717	0.09 [0.07, 0.13]	0.86 [0.84, 0.88]
Sun 2020	20	238	34	496	0.37 [0.24, 0.51]	0.68 [0.64, 0.71]
Tan 2021	45	23	242	159	0.16 [0.12, 0.20]	0.87 [0.82, 0.92]
Vieceli 2020	13	25	16	46	0.45 [0.26, 0.64]	0.65 [0.53, 0.76]
Zayet 2020a	54	69	41	53	0.57 [0.46, 0.67]	0.43 [0.34, 0.53]



Test TST-109. Nasal congestion (retrospective data collection)

Nasal congestion (retrospective data collection)

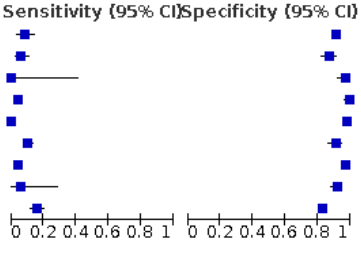
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	43	516	80	1182	0.35 [0.27, 0.44]	0.70 [0.67, 0.72]
Barbhaya 2021	110	189	736	1436	0.13 [0.11, 0.15]	0.88 [0.87, 0.90]
Chung 2021	447	1747	27	940	0.94 [0.92, 0.96]	0.35 [0.33, 0.37]
Huang 2020	11	4	325	135	0.03 [0.02, 0.06]	0.97 [0.93, 0.99]
King 2020	241	46	1746	430	0.12 [0.11, 0.14]	0.90 [0.87, 0.93]
Mao 2020	8	32	180	784	0.04 [0.02, 0.08]	0.96 [0.95, 0.97]
Martín-Sánchez 2020	16	13	424	214	0.04 [0.02, 0.06]	0.94 [0.90, 0.97]
Raberahona 2020	34	42	1254	1824	0.03 [0.02, 0.04]	0.98 [0.97, 0.98]
Wei 2020	2	0	626	308	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]



Test TST-110. Nausea or vomiting (retrospective data collection)

Nausea or vomiting (retrospective data collection)

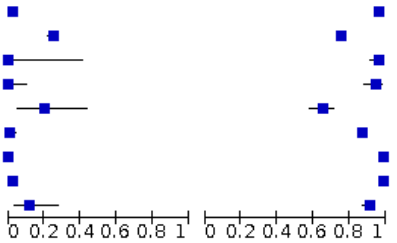
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	10	151	113	1547	0.08 [0.04, 0.14]	0.91 [0.90, 0.92]
Arslan 2021	11	30	165	198	0.06 [0.03, 0.11]	0.87 [0.82, 0.91]
Feng 2021	0	4	7	121	0.00 [0.00, 0.41]	0.97 [0.92, 0.99]
Huang 2020	14	1	322	138	0.04 [0.02, 0.07]	0.99 [0.96, 1.00]
Mao 2020	1	16	187	800	0.01 [0.00, 0.03]	0.98 [0.97, 0.99]
Martín-Sánchez 2020	45	21	395	206	0.10 [0.08, 0.13]	0.91 [0.86, 0.94]
Raberahona 2020	53	54	1235	1812	0.04 [0.03, 0.05]	0.97 [0.96, 0.98]
Sonoda 2021	1	29	16	314	0.06 [0.00, 0.29]	0.92 [0.88, 0.94]
Vilke 2020	52	1108	278	5456	0.16 [0.12, 0.20]	0.83 [0.82, 0.84]



Test TST-111. Abdominal pain (retrospective data collection)

Abdominal pain (retrospective data collection)

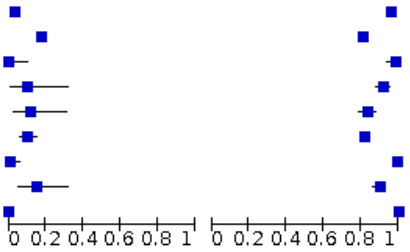
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	24	62	822	1563	0.03 [0.02, 0.04]	0.96 [0.95, 0.97]
Chung 2021	229	1011	687	3034	0.25 [0.22, 0.28]	0.75 [0.74, 0.76]
Feng 2021	0	5	7	120	0.00 [0.00, 0.41]	0.96 [0.91, 0.99]
Fiel-Ozores 2021	0	5	33	88	0.00 [0.00, 0.11]	0.95 [0.88, 0.98]
Haliga 2021	4	82	16	151	0.20 [0.06, 0.44]	0.65 [0.58, 0.71]
Lazzerini 2021	2	269	157	1720	0.01 [0.00, 0.04]	0.86 [0.85, 0.88]
Mao 2020	0	11	188	805	0.00 [0.00, 0.02]	0.99 [0.98, 0.99]
Raberahona 2020	32	26	1256	1840	0.02 [0.02, 0.03]	0.99 [0.98, 0.99]
Shah 2020	4	26	29	257	0.12 [0.03, 0.28]	0.91 [0.87, 0.94]



Test TST-112. Vomiting (retrospective data collection)

Vomiting (retrospective data collection)

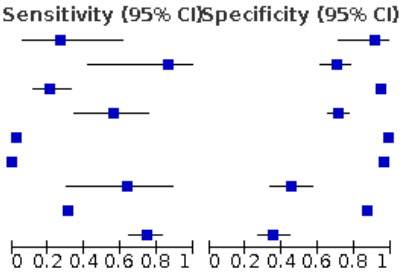
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	32	63	814	1562	0.04 [0.03, 0.05]	0.96 [0.95, 0.97]
Chung 2021	165	769	751	3276	0.18 [0.16, 0.21]	0.81 [0.80, 0.82]
Fiel-Ozores 2021	0	1	33	92	0.00 [0.00, 0.11]	0.99 [0.94, 1.00]
Haliga 2021	2	19	18	214	0.10 [0.01, 0.32]	0.92 [0.88, 0.95]
Ide 2021	3	41	22	211	0.12 [0.03, 0.31]	0.84 [0.79, 0.88]
Lazzerini 2021	16	365	143	1624	0.10 [0.06, 0.16]	0.82 [0.80, 0.83]
Leung 2021	1	12	85	1160	0.01 [0.00, 0.06]	0.99 [0.98, 0.99]
Shah 2020	5	28	28	255	0.15 [0.05, 0.32]	0.90 [0.86, 0.93]
Wei 2020	1	0	627	308	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]



Test TST-113. Myalgia or arthralgia (retrospective data collection)

Myalgia or arthralgia (retrospective data collection)

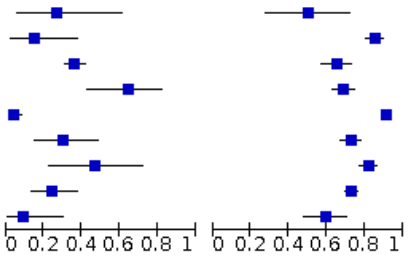
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cheng 2020	3	2	8	20	0.27 [0.06, 0.61]	0.91 [0.71, 0.99]
Feng 2021	6	37	1	88	0.86 [0.42, 1.00]	0.70 [0.62, 0.78]
Hüfner 2020	14	34	52	564	0.21 [0.12, 0.33]	0.94 [0.92, 0.96]
Ide 2021	14	72	11	180	0.56 [0.35, 0.76]	0.71 [0.65, 0.77]
King 2020	56	8	1931	468	0.03 [0.02, 0.04]	0.98 [0.97, 0.99]
Lazzerini 2021	0	71	159	1918	0.00 [0.00, 0.02]	0.96 [0.96, 0.97]
Peng 2020	7	41	4	34	0.64 [0.31, 0.89]	0.45 [0.34, 0.57]
Raberahona 2020	398	240	890	1626	0.31 [0.28, 0.34]	0.87 [0.86, 0.89]
Zayet 2020a	71	79	24	43	0.75 [0.65, 0.83]	0.35 [0.27, 0.44]



Test TST-114. Sputum production/productive cough (retrospective data collection)

Sputum production/productive cough (retrospective data collection)

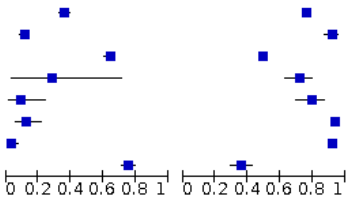
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Cheng 2020	3	11	8	11	0.27 [0.06, 0.61]	0.50 [0.28, 0.72]		
Haliga 2021	3	34	17	199	0.15 [0.03, 0.38]	0.85 [0.80, 0.90]		
Huang 2020	122	48	214	91	0.36 [0.31, 0.42]	0.65 [0.57, 0.73]		
Ide 2021	16	79	9	173	0.64 [0.43, 0.82]	0.69 [0.63, 0.74]		
Lazzerini 2021	7	185	152	1804	0.04 [0.02, 0.09]	0.91 [0.89, 0.92]		
Shah 2020	10	77	23	206	0.30 [0.16, 0.49]	0.73 [0.67, 0.78]		
Sonoda 2021	8	62	9	281	0.47 [0.23, 0.72]	0.82 [0.77, 0.86]		
Sun 2020	13	199	41	535	0.24 [0.13, 0.38]	0.73 [0.70, 0.76]		
Xie 2020	2	34	19	50	0.10 [0.01, 0.30]	0.60 [0.48, 0.70]		



Test TST-115. Chills/shivers (retrospective data collection)

Chills/shivers (retrospective data collection)

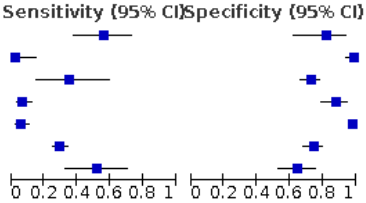
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	306	395	540	1230	0.36 [0.33, 0.40]	0.76 [0.74, 0.78]		
Chan 2021	59	17	451	194	0.12 [0.09, 0.15]	0.92 [0.87, 0.95]		
Chung 2021	586	2063	330	1982	0.64 [0.61, 0.67]	0.49 [0.47, 0.51]		
Feng 2021	2	35	5	90	0.29 [0.04, 0.71]	0.72 [0.63, 0.80]		
Fiel-Ozores 2021	3	19	30	74	0.09 [0.02, 0.24]	0.80 [0.70, 0.87]		
Leung 2021	11	75	75	1097	0.13 [0.07, 0.22]	0.94 [0.92, 0.95]		
Mao 2020	7	64	181	752	0.04 [0.02, 0.08]	0.92 [0.90, 0.94]		
Martín-Sánchez 2020	332	145	108	82	0.75 [0.71, 0.79]	0.36 [0.30, 0.43]		



Test TST-116. Asthenia (retrospective data collection)

Asthenia (retrospective data collection)

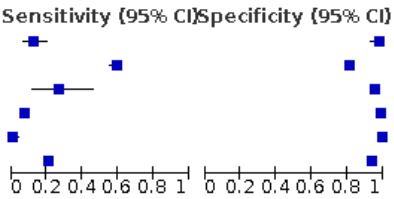
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arenas 2020	19	5	15	22	0.56 [0.38, 0.73]	0.81 [0.62, 0.94]		
Fiel-Ozores 2021	1	1	32	92	0.03 [0.00, 0.16]	0.99 [0.94, 1.00]		
Haliga 2021	7	64	13	169	0.35 [0.15, 0.59]	0.73 [0.66, 0.78]		
Langer 2020	9	9	115	66	0.07 [0.03, 0.13]	0.88 [0.78, 0.94]		
Lazzerini 2021	10	38	149	1951	0.06 [0.03, 0.11]	0.98 [0.97, 0.99]		
Martín-Sánchez 2020	131	59	309	168	0.30 [0.26, 0.34]	0.74 [0.68, 0.80]		
Vieceli 2020	15	25	14	46	0.52 [0.33, 0.71]	0.65 [0.53, 0.76]		



Test TST-117. Anosmia or ageusia (retrospective data collection)

Anosmia or ageusia (retrospective data collection)

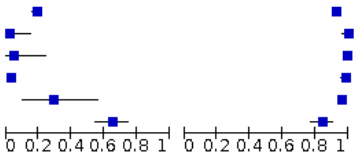
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	15	2	103	93	0.13 [0.07, 0.20]	0.98 [0.93, 1.00]		
Chung 2021	502	618	348	2634	0.59 [0.56, 0.62]	0.81 [0.80, 0.82]		
Hüfner 2020	8	23	22	434	0.27 [0.12, 0.46]	0.95 [0.93, 0.97]		
King 2020	153	5	1834	471	0.08 [0.07, 0.09]	0.99 [0.98, 1.00]		
Lazzerini 2021	2	10	157	1979	0.01 [0.00, 0.04]	0.99 [0.99, 1.00]		
Nitecki 2021	284	1451	1054	21573	0.21 [0.19, 0.24]	0.94 [0.93, 0.94]		



Test TST-118. Dysgeusia (retrospective data collection)

Dysgeusia (retrospective data collection)

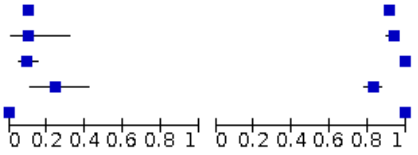
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	161	112	685	1513	0.19 [0.16, 0.22]	0.93 [0.92, 0.94]		
Fiel-Ozores 2021	1	0	32	93	0.03 [0.00, 0.16]	1.00 [0.96, 1.00]		
Haliga 2021	1	1	19	232	0.05 [0.00, 0.25]	1.00 [0.98, 1.00]		
Martín-Sánchez 2020	15	4	425	223	0.03 [0.02, 0.06]	0.98 [0.96, 1.00]		
Sonoda 2021	5	13	12	330	0.29 [0.10, 0.56]	0.96 [0.94, 0.98]		
Zayet 2020a	62	19	33	103	0.65 [0.55, 0.75]	0.84 [0.77, 0.90]		



Test TST-119. Nausea (retrospective data collection)

Nausea (retrospective data collection)

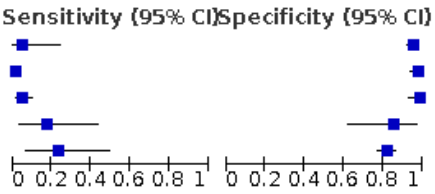
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	83	141	763	1484	0.10 [0.08, 0.12]	0.91 [0.90, 0.93]		
Haliga 2021	2	15	18	218	0.10 [0.01, 0.32]	0.94 [0.90, 0.96]		
Lazzerini 2021	15	13	144	1976	0.09 [0.05, 0.15]	0.99 [0.99, 1.00]		
Shah 2020	8	48	25	235	0.24 [0.11, 0.42]	0.83 [0.78, 0.87]		
Wei 2020	1	1	627	307	0.00 [0.00, 0.01]	1.00 [0.98, 1.00]		



Test TST-120. Arthralgia (retrospective data collection)

Arthralgia (retrospective data collection)

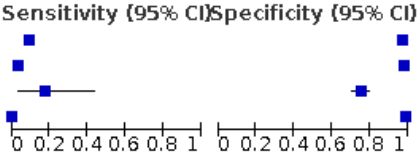
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	1	11	19	222	0.05 [0.00, 0.25]	0.95 [0.92, 0.98]		
Huang 2020	6	3	330	136	0.02 [0.01, 0.04]	0.98 [0.94, 1.00]		
Langer 2020	6	1	118	74	0.05 [0.02, 0.10]	0.99 [0.93, 1.00]		
Pisapia 2020	3	3	14	17	0.18 [0.04, 0.43]	0.85 [0.62, 0.97]		
Sonoda 2021	4	62	13	281	0.24 [0.07, 0.50]	0.82 [0.77, 0.86]		



Test TST-121. Anorexia (retrospective data collection)

Anorexia (retrospective data collection)

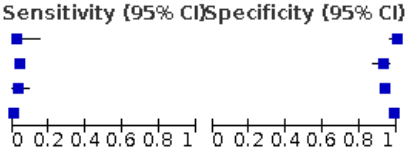
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	76	50	770	1575	0.09 [0.07, 0.11]	0.97 [0.96, 0.98]		
King 2020	75	10	1912	466	0.04 [0.03, 0.05]	0.98 [0.96, 0.99]		
Sonoda 2021	3	85	14	258	0.18 [0.04, 0.43]	0.75 [0.70, 0.80]		
Wei 2020	3	4	625	304	0.00 [0.00, 0.01]	0.99 [0.97, 1.00]		



Test TST-122. Wheeze (retrospective data collection)

Wheeze (retrospective data collection)

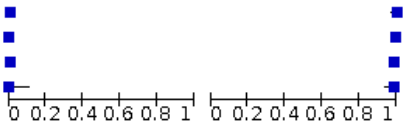
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	1	0	32	93	0.03 [0.00, 0.16]	1.00 [0.96, 1.00]		
Huang 2020	15	10	321	129	0.04 [0.03, 0.07]	0.93 [0.87, 0.96]		
Lazzerini 2021	3	120	83	1706	0.03 [0.01, 0.10]	0.93 [0.92, 0.95]		
Raberahona 2020	10	29	1278	1837	0.01 [0.00, 0.01]	0.98 [0.98, 0.99]		



Test TST-123. Haemoptysis (retrospective data collection)

Haemoptysis (retrospective data collection)

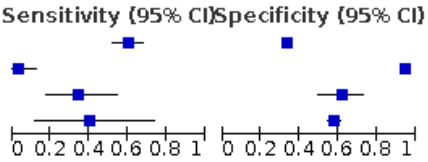
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	3	0	333	139	0.01 [0.00, 0.03]	1.00 [0.97, 1.00]
Mao 2020	1	7	187	809	0.01 [0.00, 0.03]	0.99 [0.98, 1.00]
Raberahona 2020	16	26	1272	1840	0.01 [0.01, 0.02]	0.99 [0.98, 0.99]
Zhu 2020	0	1	32	83	0.00 [0.00, 0.11]	0.99 [0.94, 1.00]



Test TST-124. Respiratory symptoms (not specified; retrospective data collection)

Respiratory symptoms (not specified; retrospective data collection)

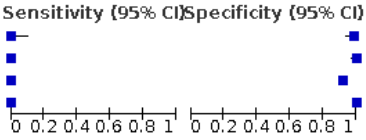
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lazzerini 2021	96	1325	63	664	0.60 [0.52, 0.68]	0.33 [0.31, 0.36]
Sun 2020	2	43	52	691	0.04 [0.00, 0.13]	0.94 [0.92, 0.96]
Vieceli 2020	10	27	19	44	0.34 [0.18, 0.54]	0.62 [0.50, 0.73]
Zurl 2021	4	458	6	632	0.40 [0.12, 0.74]	0.58 [0.55, 0.61]



Test TST-125. Skin lesions (retrospective data collection)

Skin lesions (retrospective data collection)

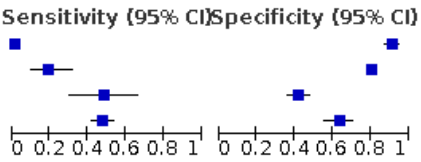
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	0	1	33	92	0.00 [0.00, 0.11]	0.99 [0.94, 1.00]
Huang 2020	0	0	336	139	0.00 [0.00, 0.01]	1.00 [0.97, 1.00]
Lazzerini 2021	0	158	159	1831	0.00 [0.00, 0.02]	0.92 [0.91, 0.93]
Martín-Sánchez 2020	0	0	440	227	0.00 [0.00, 0.01]	1.00 [0.98, 1.00]



Test TST-126. Tachycardia (retrospective data collection)

Tachycardia (retrospective data collection)

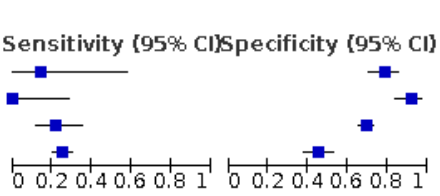
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	3	20	173	208	0.02 [0.00, 0.05]	0.91 [0.87, 0.95]
Lazzerini 2021	12	294	49	1195	0.20 [0.11, 0.32]	0.80 [0.78, 0.82]
Shah 2020	16	164	17	119	0.48 [0.31, 0.66]	0.42 [0.36, 0.48]
Tan 2021	137	67	150	115	0.48 [0.42, 0.54]	0.63 [0.56, 0.70]



Test TST-127. Nasal symptoms (retrospective data collection)

Nasal symptoms (retrospective data collection)

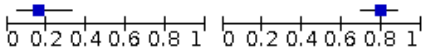
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Feng 2021	1	27	6	98	0.14 [0.00, 0.58]	0.78 [0.70, 0.85]
Peng 2020	0	6	11	69	0.00 [0.00, 0.28]	0.92 [0.83, 0.97]
Sun 2020	12	226	42	508	0.22 [0.12, 0.36]	0.69 [0.66, 0.73]
Tan 2021	72	100	215	82	0.25 [0.20, 0.31]	0.45 [0.38, 0.53]



Test TST-128. Expectoration (retrospective data collection)

Expectoration (retrospective data collection)

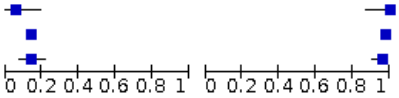
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Feng 2021	2	36	4	89	0.33 [0.04, 0.78]	0.71 [0.62, 0.79]		
Vieceli 2020	3	17	26	54	0.10 [0.02, 0.27]	0.76 [0.64, 0.85]		
Wei 2020	1	0	627	308	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]		
Zhu 2020	5	17	27	67	0.16 [0.05, 0.33]	0.80 [0.70, 0.88]		



Test TST-129. Ageusia (retrospective data collection)

Ageusia (retrospective data collection)

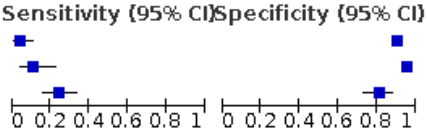
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arenas 2020	2	0	32	27	0.06 [0.01, 0.20]	1.00 [0.87, 1.00]		
Raberahona 2020	185	38	1103	1828	0.14 [0.12, 0.16]	0.98 [0.97, 0.99]		
Tordjman 2020	14	4	86	96	0.14 [0.08, 0.22]	0.96 [0.90, 0.99]		



Test TST-130. Positive auscultation findings (retrospective data collection)

Positive auscultation findings (retrospective data collection)

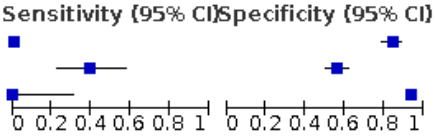
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Lazzerini 2021	4	186	82	1640	0.05 [0.01, 0.11]	0.90 [0.88, 0.91]		
Sun 2020	6	36	48	698	0.11 [0.04, 0.23]	0.95 [0.93, 0.97]		
Zayet 2020a	23	23	72	99	0.24 [0.16, 0.34]	0.81 [0.73, 0.88]		



Test TST-131. Tachypnea (retrospective data collection)

Tachypnea (retrospective data collection)

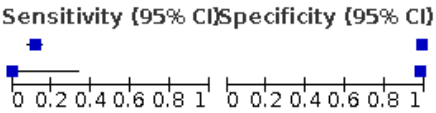
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	2	36	174	192	0.01 [0.00, 0.04]	0.84 [0.79, 0.89]		
Shah 2020	13	124	20	159	0.39 [0.23, 0.58]	0.56 [0.50, 0.62]		
Zurl 2021	0	66	10	960	0.00 [0.00, 0.31]	0.94 [0.92, 0.95]		



Test TST-132. Anosmia/dysosmia or ageusia/dysgeusia (retrospective data collection))

Anosmia/dysosmia or ageusia/dysgeusia (retrospective data collection))

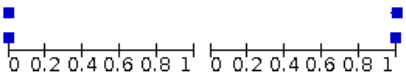
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	38	109	292	6455	0.12 [0.08, 0.15]	0.98 [0.98, 0.99]		
Zurl 2021	0	16	9	603	0.00 [0.00, 0.34]	0.97 [0.96, 0.99]		



Test TST-133. Earache (retrospective data collection)

Earache (retrospective data collection)

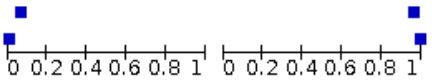
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	1	0	335	139	0.00 [0.00, 0.02]	1.00 [0.97, 1.00]
Raberahona 2020	7	15	1281	1851	0.01 [0.00, 0.01]	0.99 [0.99, 1.00]



Test TST-134. Sneezing (retrospective data collection)

Sneezing (retrospective data collection)

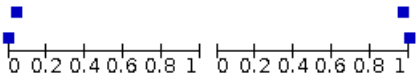
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
King 2020	132	18	1855	458	0.07 [0.06, 0.08]	0.96 [0.94, 0.98]
Mao 2020	2	2	186	814	0.01 [0.00, 0.04]	1.00 [0.99, 1.00]



Test TST-135. Dizziness (retrospective data collection)

Dizziness (retrospective data collection)

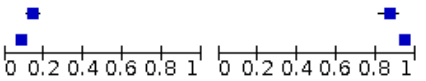
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	36	50	810	1575	0.04 [0.03, 0.06]	0.97 [0.96, 0.98]
Wei 2020	1	0	627	308	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]



Test TST-136. Malaise (retrospective data collection)

Malaise (retrospective data collection)

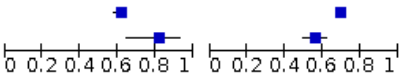
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chan 2021	74	28	436	183	0.15 [0.12, 0.18]	0.87 [0.81, 0.91]
King 2020	165	25	1822	451	0.08 [0.07, 0.10]	0.95 [0.92, 0.97]



Test TST-137. Fever (subjective) (retrospective data collection)

Fever (subjective) (retrospective data collection)

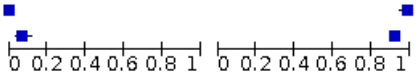
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Barbhaya 2021	520	498	326	1127	0.61 [0.58, 0.65]	0.69 [0.67, 0.72]
Shah 2020	27	125	6	158	0.82 [0.65, 0.93]	0.56 [0.50, 0.62]



Test TST-138. Enlargement of lymph nodes (retrospective data collection)

Enlargement of lymph nodes (retrospective data collection)

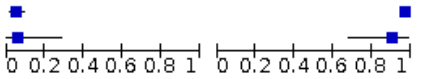
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	0	2	336	137	0.00 [0.00, 0.01]	0.99 [0.95, 1.00]
Lazzerini 2021	11	158	148	1831	0.07 [0.04, 0.12]	0.92 [0.91, 0.93]



Test TST-139. Conjunctivitis (retrospective data collection)

Conjunctivitis (retrospective data collection)

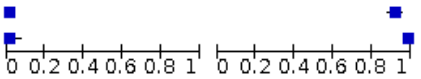
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Lazzerini 2021	8	60	151	1929	0.05 [0.02, 0.10]	0.97 [0.96, 0.98]		
Pisapia 2020	1	2	16	18	0.06 [0.00, 0.29]	0.90 [0.68, 0.99]		



Test TST-140. Hypoxia (retrospective data collection)

Hypoxia (retrospective data collection)

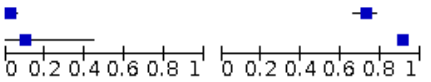
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	3	18	173	210	0.02 [0.00, 0.05]	0.92 [0.88, 0.95]		
Lazzerini 2021	1	21	65	1554	0.02 [0.00, 0.08]	0.99 [0.98, 0.99]		



Test TST-141. Pulmonary auscultation: rhonchi (retrospective data collection)

Pulmonary auscultation: rhonchi (retrospective data collection)

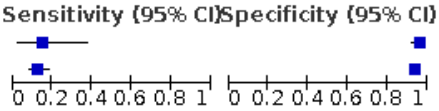
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	5	63	171	165	0.03 [0.01, 0.07]	0.72 [0.66, 0.78]		
Zurl 2021	1	88	9	942	0.10 [0.00, 0.45]	0.91 [0.90, 0.93]		



Test TST-142. Loss of appetite (retrospective data collection)

Loss of appetite (retrospective data collection)

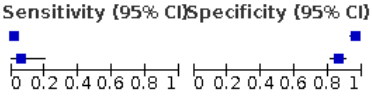
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	3	10	17	223	0.15 [0.03, 0.38]	0.96 [0.92, 0.98]		
Mao 2020	24	55	164	761	0.13 [0.08, 0.18]	0.93 [0.91, 0.95]		



Test TST-143. Altered mentation/confusion (retrospective data collection)

Altered mentation/confusion (retrospective data collection)

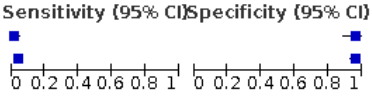
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Martín-Sánchez 2020	9	9	431	218	0.02 [0.01, 0.04]	0.96 [0.93, 0.98]		
Shah 2020	2	39	31	244	0.06 [0.01, 0.20]	0.86 [0.82, 0.90]		



Test TST-144. Presyncope or syncope (retrospective data collection)

Presyncope or syncope (retrospective data collection)

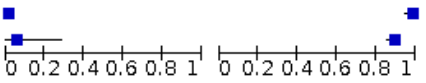
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Langer 2020	2	3	122	72	0.02 [0.00, 0.06]	0.96 [0.89, 0.99]		
Martín-Sánchez 2020	21	9	419	218	0.05 [0.03, 0.07]	0.96 [0.93, 0.98]		



Test TST-145. Stomach ache (retrospective data collection)

Stomach ache (retrospective data collection)

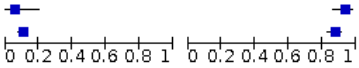
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	6	2	330	137	0.02 [0.01, 0.04]	0.99 [0.95, 1.00]		
Sonoda 2021	1	37	16	306	0.06 [0.00, 0.29]	0.89 [0.85, 0.92]		



Test TST-146. Odynophagia (retrospective data collection)

Odynophagia (retrospective data collection)

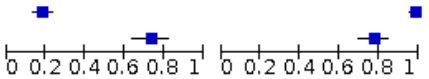
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	2	6	31	87	0.06 [0.01, 0.20]	0.94 [0.86, 0.98]		
Martín-Sánchez 2020	47	28	393	199	0.11 [0.08, 0.14]	0.88 [0.83, 0.92]		



Test TST-147. Anosmia or dysgeusia (retrospective data collection)

Anosmia or dysgeusia (retrospective data collection)

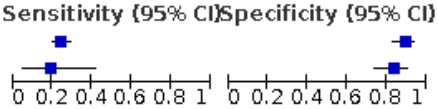
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Tan 2021	53	3	234	179	0.18 [0.14, 0.23]	0.98 [0.95, 1.00]		
Zayet 2020a	70	27	25	95	0.74 [0.64, 0.82]	0.78 [0.69, 0.85]		



Test TST-148. Weakness or fatigue (retrospective data collection)

Weakness or fatigue (retrospective data collection)

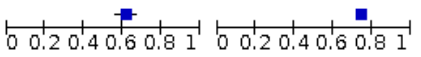
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	83	15	253	124	0.25 [0.20, 0.30]	0.89 [0.83, 0.94]		
Xie 2020	4	14	17	70	0.19 [0.05, 0.42]	0.83 [0.74, 0.91]		



Test TST-149. Objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Objective fever (≥ 38 °C) or recent fever/chills (retrospective)

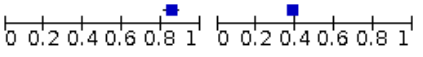
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	203	1679	127	4885	0.62 [0.56, 0.67]	0.74 [0.73, 0.75]		



Test TST-150. Body aches or fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Body aches or fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	282	4045	48	2519	0.85 [0.81, 0.89]	0.38 [0.37, 0.40]		



Test TST-151. Fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Fatigue or dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	280	4001	50	2563	0.85 [0.81, 0.89]	0.39 [0.38, 0.40]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-152. Dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Dyspnoea or cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	274	3430	56	3134	0.83 [0.79, 0.87]	0.48 [0.47, 0.49]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-153. Cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Cough or objective fever (≥ 38 °C) or recent fever/chills (retrospective)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	266	2680	64	3884	0.81 [0.76, 0.85]	0.59 [0.58, 0.60]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-154. Recent fever or chills (retrospective data collection)

Recent fever or chills (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	193	1608	137	4956	0.58 [0.53, 0.64]	0.76 [0.74, 0.77]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-155. Sinusitis (retrospective data collection)

Sinusitis (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	31	266	299	6298	0.09 [0.06, 0.13]	0.96 [0.95, 0.96]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-156. Systemic soreness (malaise/myalgia/arthralgia) (retrospective)

Systemic soreness (malaise/myalgia/arthralgia) (retrospective)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vilke 2020	59	420	271	6144	0.18 [0.14, 0.22]	0.94 [0.93, 0.94]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-157. Malaise or fatigue (retrospective data collection)

Malaise or fatigue (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Raberahona 2020	403	303	885	1563	0.31 [0.29, 0.34]	0.84 [0.82, 0.85]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-158. Lethargy (retrospective data collection)

Lethargy (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ahmed 2021	40	461	83	1237	0.33 [0.24, 0.42]	0.73 [0.71, 0.75]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-159. Nausea or vomiting or diarrhoea (retrospective data collection)

Nausea or vomiting or diarrhoea (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Sacks 2020	38	258	119	1332	0.24 [0.18, 0.32]	0.84 [0.82, 0.86]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-160. Respiratory triage score > 4 (retrospective data collection)

Respiratory triage score > 4 (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Aldobyany 2020	224	557	116	538	0.66 [0.61, 0.71]	0.49 [0.46, 0.52]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-161. Respiratory triage score > 5 (retrospective data collection)

Respiratory triage score > 5 (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Aldobyany 2020	218	485	122	610	0.64 [0.59, 0.69]	0.56 [0.53, 0.59]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-162. Lower respiratory tract symptoms (retrospective data collection)

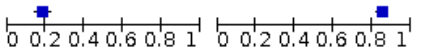
Lower respiratory tract symptoms (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Simpson 2020	13	54	365	778	0.03 [0.02, 0.06]	0.94 [0.92, 0.95]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Test TST-163. Neurologic symptoms (not specified; retrospective data collection)

Neurologic symptoms (not specified; retrospective data collection)

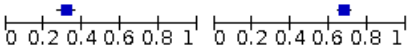
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Simpson 2020	71	124	307	708	0.19 [0.15, 0.23]	0.85 [0.82, 0.87]		



Test TST-164. Upper respiratory tract symptoms (retrospective data collection)

Upper respiratory tract symptoms (retrospective data collection)

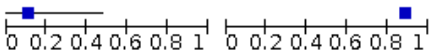
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Simpson 2020	119	266	259	566	0.31 [0.27, 0.36]	0.68 [0.65, 0.71]		



Test TST-165. Laryngitis/hoarseness/stridor (retrospective data collection)

Laryngitis/hoarseness/stridor (retrospective data collection)

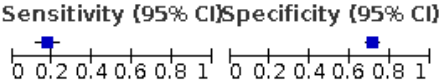
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Zurl 2021	1	119	8	923	0.11 [0.00, 0.48]	0.89 [0.86, 0.90]		



Test TST-166. High fever (≥ 38.5 °C) (retrospective data collection)

High fever (≥ 38.5 °C) (retrospective data collection)

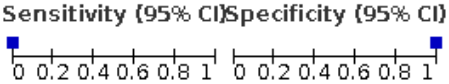
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Mao 2020	33	234	155	582	0.18 [0.12, 0.24]	0.71 [0.68, 0.74]		



Test TST-167. Abdominal distention (retrospective data collection)

Abdominal distention (retrospective data collection)

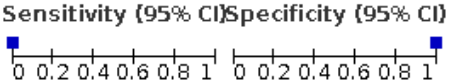
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	0	1	628	307	0.00 [0.00, 0.01]	1.00 [0.98, 1.00]		



Test TST-168. Aversion to cold (retrospective data collection)

Aversion to cold (retrospective data collection)

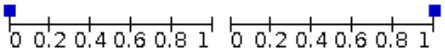
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	1	1	627	307	0.00 [0.00, 0.01]	1.00 [0.98, 1.00]		



Test TST-169. Xerostomia (retrospective data collection)

Xerostomia (retrospective data collection)

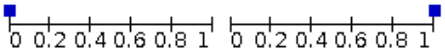
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	1	0	627	308	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]		



Test TST-170. Hypersomnia (retrospective data collection)

Hypersomnia (retrospective data collection)

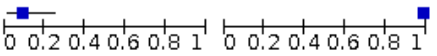
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2020	1	0	627	308	0.00 [0.00, 0.01]	1.00 [0.99, 1.00]		



Test TST-171. Hyposmia (retrospective data collection)

Hyposmia (retrospective data collection)

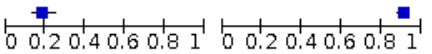
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Chua 2020	3	8	28	678	0.10 [0.02, 0.26]	0.99 [0.98, 0.99]		



Test TST-172. Fever and cough and dyspnoea (retrospective)

Fever and cough and dyspnoea (retrospective)

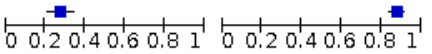
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Yombi 2020	33	31	142	330	0.19 [0.13, 0.25]	0.91 [0.88, 0.94]		



Test TST-173. Fever and cough and sore throat (retrospective)

Fever and cough and sore throat (retrospective)

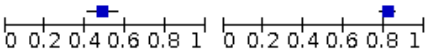
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Yombi 2020	48	44	127	317	0.27 [0.21, 0.35]	0.88 [0.84, 0.91]		



Test TST-174. Fever and cough (retrospective data collection)

Fever and cough (retrospective data collection)

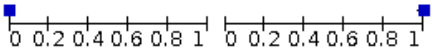
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Yombi 2020	85	65	90	296	0.49 [0.41, 0.56]	0.82 [0.78, 0.86]		



Test TST-175. Unconsciousness (retrospective data collection)

Unconsciousness (retrospective data collection)

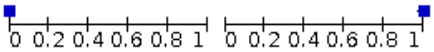
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	1	0	335	139	0.00 [0.00, 0.02]	1.00 [0.97, 1.00]		



Test TST-176. Rash (retrospective data collection)

Rash (retrospective data collection)

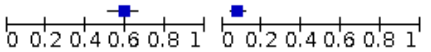
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang 2020	2	0	334	139	0.01 [0.00, 0.02]	1.00 [0.97, 1.00]		



Test TST-177. Fever or cough or dyspnoea (retrospective data collection)

Fever or cough or dyspnoea (retrospective data collection)

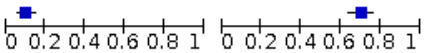
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	104	210	72	18	0.59 [0.51, 0.66]	0.08 [0.05, 0.12]		



Test TST-178. Pulmonary auscultation: crackling (retrospective data collection)

Pulmonary auscultation: crackling (retrospective data collection)

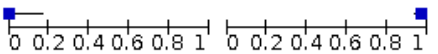
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arslan 2021	18	68	158	160	0.10 [0.06, 0.16]	0.70 [0.64, 0.76]		



Test TST-179. Dysphonia (retrospective data collection)

Dysphonia (retrospective data collection)

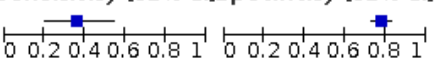
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	0	7	20	226	0.00 [0.00, 0.17]	0.97 [0.94, 0.99]		



Test TST-180. Dry cough (retrospective data collection)

Dry cough (retrospective data collection)

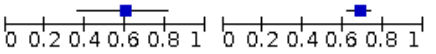
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Shah 2020	12	62	21	221	0.36 [0.20, 0.55]	0.78 [0.73, 0.83]		



Test TST-181. History of fever at home (retrospective data collection)

History of fever at home (retrospective data collection)

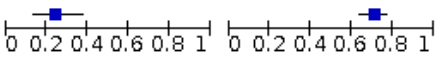
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Haliga 2021	12	74	8	159	0.60 [0.36, 0.81]	0.68 [0.62, 0.74]		



Test TST-182. Cough or dyspnoea (retrospective data collection)

Cough or dyspnoea (retrospective data collection)

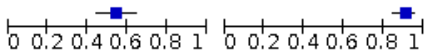
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kim 2020	13	55	41	133	0.24 [0.13, 0.38]	0.71 [0.64, 0.77]		



Test TST-183. Anosmia and dysgeusia (retrospective data collection)

Anosmia and dysgeusia (retrospective data collection)

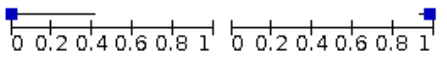
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Zayet 2020a	52	11	43	111	0.55 [0.44, 0.65]	0.91 [0.84, 0.95]		



Test TST-184. Palpitations (retrospective data collection)

Palpitations (retrospective data collection)

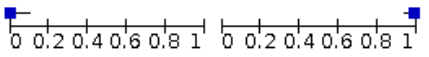
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Feng 2021	0	3	7	122	0.00 [0.00, 0.41]	0.98 [0.93, 1.00]		



Test TST-185. Anosmia or hyposmia (retrospective data collection)

Anosmia or hyposmia (retrospective data collection)

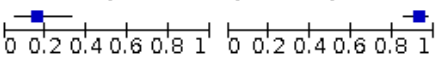
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Fiel-Ozores 2021	0	1	33	92	0.00 [0.00, 0.11]	0.99 [0.94, 1.00]		



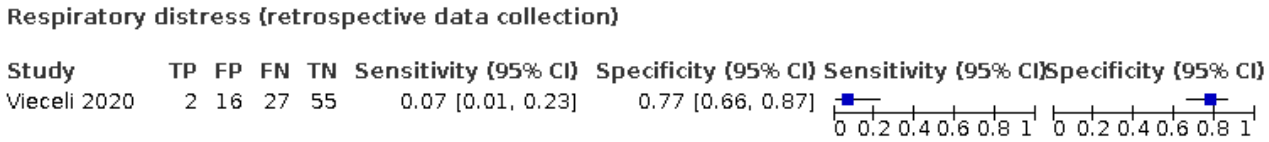
Test TST-186. Myalgia or fatigue (retrospective data collection)

Myalgia or fatigue (retrospective data collection)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Zhu 2020	5	6	27	78	0.16 [0.05, 0.33]	0.93 [0.85, 0.97]		



Test TST-187. Respiratory distress (retrospective data collection)



ADDITIONAL TABLES

Table 1. QUADAS-2 checklist

Index test(s)	Signs and symptoms
Patients (setting, intended use of index test, presentation, prior testing)	Primary care, hospital outpatient settings including emergency departments Inpatients presenting with suspected COVID-19 No prior testing Signs and symptoms often used for triage or referral
Reference standard and target condition	The focus will be on the diagnosis of COVID-19 disease and COVID-19 pneumonia. For this review, the focus will not be on prognosis.
Participant selection	
Was a consecutive or random sample of patients enrolled?	This will be similar for all index tests, target conditions, and populations. YES: if a study explicitly stated that all participants within a certain time frame were included; that this was done consecutively; or that a random selection was done. NO: if it was clear that a different selection procedure was employed; for example, selection based on clinician's preference, or based on institutions. UNCLEAR: if the selection procedure was not clear or not reported.
Was a case-control design avoided?	This will be similar for all index tests, target conditions, and populations. YES: if a study explicitly stated that all participants came from the same group of (suspected) patients. NO: if it was clear that a different selection procedure was employed for the participants depending on their COVID-19 (pneumonia) status or SARS-CoV-2 infection status. UNCLEAR: if the selection procedure was not clear or not reported.
Did the study avoid inappropriate exclusions?	Studies may have excluded participants, or selected participants in such a way that they avoided including those who were difficult to diagnose or likely to be borderline. Although the inclusion and exclusion criteria will be different for the different index tests, inappropriate exclusions and inclusions will be similar for all index tests: for example, only elderly patients excluded, or children (as sampling may be more difficult). This needs to be addressed on a case-by-case basis. YES: if a high proportion of eligible patients was included without clear selection. NO: if a high proportion of eligible patients was excluded without providing a reason; if, in a retrospective study, participants without index test or reference standard results were excluded; if exclusion was based on severity assessment post-factum or comorbidities (cardiovascular disease, diabetes, immunosuppression).

Table 1. QUADAS-2 checklist *(Continued)*

	UNCLEAR: if the exclusion criteria were not reported.
Did the study avoid inappropriate inclusions?	YES: if samples included were likely to be representative of the spectrum of disease. NO: if the study oversampled patients with particular characteristics likely to affect estimates of accuracy. UNCLEAR: if the exclusion criteria were not reported.
Could the selection of patients have introduced bias?	HIGH: if one or more signalling questions were answered with NO, as any deviation from the selection process may lead to bias. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.
Is there concern that the included patients do not match the review question?	HIGH: if accuracy of signs and symptoms were assessed in a case-control design, or in an already highly selected group of participants, or the study was able to only estimate sensitivity or specificity. LOW: any situation where signs and symptoms were the first assessment/test to be done on the included participants. UNCLEAR: if a description about the participants was lacking.
Index tests	
Were the index test results interpreted without knowledge of the results of the reference standard?	This will be similar for all index tests, target conditions, and populations. YES: if blinding was explicitly stated or index test was recorded before the results from the reference standard were available. NO: if it was explicitly stated that the index test results were interpreted with knowledge of the results of the reference standard. UNCLEAR: if blinding was unclearly reported.
If a threshold was used, was it prespecified?	This will be similar for all index tests, target conditions, and populations. YES: if the test was dichotomous by nature, or if the threshold was stated in the methods section, or if authors stated that the threshold as recommended by the manufacturer was used. NO: if a receiver operating characteristic curve was drawn or multiple threshold reported in the results section; and the final result was based on one of these thresholds; if fever was not defined beforehand. UNCLEAR: if threshold selection was not clearly reported.
Could the conduct or interpretation of the index test have introduced bias?	HIGH: if one or more signalling questions were answered with NO, as even in a laboratory situation knowledge of the reference standard may lead to bias. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.
Is there concern that the index test, its conduct, or interpretation differ from the review question?	This will probably be answered 'LOW' in all cases except when assessments were made in a different setting, or using personnel not available in practice.
Reference standard	

Table 1. QUADAS-2 checklist *(Continued)*

Is the reference standard likely to correctly classify the target condition?	We will define acceptable reference standards using a consensus process once the list of reference standards that have been used has been obtained from the eligible studies. For severe pneumonia, we will consider how well processes adhered to the WHO case definition in Appendix 1 .
Were the reference standard results interpreted without knowledge of the results of the index test?	YES: if it was explicitly stated that the reference standard results were interpreted without knowledge of the results of the index test, or if the result of the index test was obtained after the reference standard. NO: if it was explicitly stated that the reference standard results were interpreted with knowledge of the results of the index test or if the index test was used to make the final diagnosis. UNCLEAR: if blinding was unclearly reported.
Did the definition of the reference standard incorporate results from the index test(s)?	YES: if results from the index test were a component of the reference standard definition. NO: if the reference standard did not incorporate the index standard test. UNCLEAR: if it was unclear whether the results of the index test formed part of the reference standard.
Could the conduct or interpretation of the reference standard have introduced bias?	HIGH: if one or more signalling questions were answered with NO. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.
Is there concern that the target condition as defined by the reference standard does not match the review question?	HIGH: if the target condition was COVID-19 pneumonia, but only RT-PCR was used; if alternative diagnosis was highly likely and not excluded (will happen in paediatric cases, where exclusion of other respiratory pathogens is also necessary); if tests used to follow up viral load in known test-positives. LOW: if above situations were not present. UNCLEAR: if intention for testing was not reported in the study.
Flow and timing	
Was there an appropriate interval between index test(s) and reference standard?	YES: this will be similar for all index tests, populations for the current infection target conditions: as the situation of a patient, including clinical presentation and disease progress, evolves rapidly and new/ongoing exposure can result in case status change, an appropriate time interval will be within 24 h. NO: if there was more than 24 h between the index test and the reference standard or if participants were otherwise reported to be assessed with the index versus reference standard test at moments of different severity. UNCLEAR: if the time interval was not reported.
Did all patients receive a reference standard?	YES: if all participants received a reference standard (clearly no partial verification). NO: if only (part of) the index test-positives or index test-negatives received the complete reference standard. UNCLEAR: if it was not reported.
Did all patients receive the same reference standard?	YES: if all participants received the same reference standard (clearly no differential verification). NO: if (part of) the index test-positives or index test-negatives received a different reference standard.

Table 1. QUADAS-2 checklist *(Continued)*

	UNCLEAR: if it was not reported.
Were all patients included in the analysis?	YES: if all included participants were included in the analyses. NO: if after the inclusion/exclusion process, participants were removed from the analyses for different reasons: no reference standard done, no index test done, intermediate results of both index test or reference standard, indeterminate results of both index test or reference standard, samples unusable. UNCLEAR: if this was not clear from the reported numbers.
Could the patient flow have introduced bias?	HIGH: if one or more signalling questions were answered with NO. LOW: if all signalling questions were answered with YES. UNCLEAR: all other instances.

ICU: intensive care unit; **RT-PCR:** reverse transcription polymerase chain reaction; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **WHO:** World Health Organization

Table 2. Study characteristics (cross-sectional prospective studies only)

Study ID	Target condition	Sample size	Prevalence	Country	Setting	Population	Reference standard
Alizadehsani 2021	COVID-19 pneumonia	319	39%	Iran	ED	All patients referred to the imaging department on suspicion of COVID-19 (with flu-like symptoms)	Thin-slice high-resolution multi-slice spiral CT scan in a supine position, and high-resolution CT images
Bhattacharya 2021	COVID-19	378	33%	India	ED	Patients who were suspected of COVID-19. From 1066 suspected patients who were tested during this period, 384 patients were enrolled in the study based on the availability of informed consent and successful telephonic communication. Suspicion based on the testing advisory developed by the Indian Council of Medical Research (ICMR), Version 5, dated May 18, 2020. "ILI symptoms", defined as acute respiratory infection with fever ≥ 38 °C AND cough	RT-PCR for SARS-CoV-2 (nasal + throat swab)
Bouzid 2020	COVID-19	596	45%	France	ED	All consecutive patients presenting with an influenza-like illness (ILI: fever with a temperature > 38.5°C, malaise, headache, and myalgia; and 1 respiratory symptom (cough, sore throat, and dyspnoea)) and admitted to the hospital through the ED	Either with QIAstat-Dx Respiratory SARS-CoV-2 Panel or with a combination of the RT-PCR RealStar SARS-CoV-2 Kit RUO and rapid multiplex PCR FilmArray RP2; specimen not specified
Brendish 2020	COVID-19	1054	33%	UK	ED	All consecutive adults presenting with an acute respiratory illness or otherwise clinically suspected of having COVID-19	Either laboratory RT-PCR or MPOCT (QIAGEN) for SARS-CoV-2 (nasopharyngeal swab)
Buonafine 2020	COVID-19	295	42%	Brazil	Outpatient setting	HCW with self-reported fever or any of the following: acute respiratory symptoms (cough, nasal congestion, sore throat, shortness of breath), loss or changed sense of	RT-PCR for SARS-CoV-2 (nasopharyngeal and oropharyngeal swab)

Table 2. Study characteristics (cross-sectional prospective studies only) *(Continued)*

						smell or taste, ocular symptoms, headache, arthralgia, myalgia, fatigue, diarrhoea, nausea, and vomiting	
Clemency 2020	COVID-19	961	23%	USA	Outpatient setting	HCWs triaged by phone, tested at drive-through site	RT-PCR on nasopharyngeal or oropharyngeal swabs
Drager 2020	COVID-19	2257	7%	Germany	Outpatient setting	All patients presenting themselves at the outpatient clinic: patients with symptoms (not further specified) + high-risk contacts or returning from a high-risk area were tested for SARS-CoV-2	Not specified (throat swab)
Fink 2021	COVID-19/ COVID-19 pneumonia	219	33%	Germany	ED	Patients who presented at ED with signs of a respiratory infection suspicious for COVID-19 and received radiological imaging as well as RT-PCR for SARS-CoV-2	RT-PCR for SARS-CoV-2 (nasopharyngeal and oropharyngeal swab)
Gilbert 2020	COVID-19	598	29%	Belgium	Outpatient setting	Suspected patients sent to testing centres close to ED	RT-PCR on nasopharyngeal swabs
Haehner 2020	COVID-19	500	7%	Germany	Outpatient setting	Patients presenting with symptoms of a common cold to a corona testing centre	RT-PCR on throat swabs
Ishii 2021	COVID-19	3540	5%	Japan	Outpatient setting	All consecutive participants who underwent drive-through nasopharyngeal swab testing at an outpatient clinic. Reason for testing: upon request of the participant or participants who had been confirmed to have contacted COVID-19 patients based on contact tracing. No clinical suspicion needed per se, but 54% of individuals were symptomatic, suggestive of COVID-19	RT-PCR, nasopharyngeal swab
Jeyashree 2021	COVID-19	277	21%	India	Outpatient setting	All consecutive adults who visited COVID-19 testing centres in Chennai city in Southern India	RT-PCR, nasopharyngeal swab
Just 2020	COVID-19	374	11%	Germany	Primary care	Convenience sample of patients who were tested in GPs' practices	RT-PCR, samples not specified

Table 2. Study characteristics (cross-sectional prospective studies only) *(Continued)*

Kalayjian 2020	COVID-19	345	34%	USA	Outpatient setting	Clients entering the health centre (walk-in clinic) were screened for symptoms and triaged to the COVID-19 clinic. Testing was performed for patients with a documented or subjective fever within the past 72 h.	Labcorp's nucleic-acid amplification, threshold not specified, nasopharyngeal swabs
Kempker 2020	COVID-19	283	18%	USA	Outpatient setting	HCWs with a viral-like illness, triaged to the employee health services staff for a virtual clinical assessment and then scheduled for SARS-CoV-2 testing	RT-PCR, nasopharyngeal swab
Krastinova 2020	COVID-19	314	110	France	Outpatient setting	Symptomatic HCWs, defined as the presence of fever and/or respiratory symptoms	RT-PCR, nasopharyngeal swabs
Leal 2020	COVID-19	1583	28%	Brazil	Outpatient setting	Patients meeting the suspected COVID-19 case definition (tested after initial screening questionnaire)	RT-PCR, samples not specified
Maechler 2020	COVID-19	4333	8%	Germany	Outpatient setting	Until 24 March 2020: symptomatic patients with high-risk contacts or return from high-risk area. From 24 March: also symptomatic people with risk factors and if the test capacity allowed also only symptomatic patients. Plus 2 subgroups of high-risk patients in a nightclub and Charité employees	SARS-CoV-2 RT-PCR test (combined oro- and nasopharyngeal swab)
Mansella 2020	COVID-19	4815	12%	Switzerland	Outpatient setting	All patients presenting at the test centre with respiratory symptoms (such as shortness of breath), other flu-like symptoms (fever, sore throat, cough) and self-reported exposure to COVID-19	RT-PCR, 2 swabs from naso- and oropharyngeal sites combined into 1
Martin-Sanz 2020	COVID-19	355	61%	Spain	Outpatient setting	HCWs with suspicion of COVID-19 infection. Suspicion of COVID-19 was determined by the presence of either cough, fever (> 37.5 °C), headache, or breathlessness, regardless of contact with a COVID-19 patient	SARS-CoV-2 next-generation sequencing or real-time (RT)-PCR methods (nasal- and pharyngeal swabs)
Nazerian 2021	COVID-19	838	23%	Italy	ED	Patients with suspected COVID-19 were prospectively enrolled in 2 EDs	RT-PCR, positive result within 5 days after ED presentation, *or* sugges-

Table 2. Study characteristics (cross-sectional prospective studies only) *(Continued)*

							tive symptoms plus chest imaging (showing acute interstitial lung disease in the absence of an alternative diagnosis), *or* panel adjudication (for 3 cases without a positive PCR)
Olivar Lopez 2020	COVID-19	510	15%	Mexico	ED	All patients < 18 years who presented with a clinical picture compatible with COVID-19 (= fever, respiratory symptoms or general malaise) at the ED of a COVID paediatric reference hospital	RT-PCR, nasopharyngeal swabs
O'Reilly 2020a	COVID-19	240	5%	Australia	ED	Patients who meet the testing criteria for COVID-19 and who present at the ED	RT-PCR, sample not specified
O'Reilly 2020b	COVID-19	1334	4%	Australia	ED	All adult patients who met criteria for "suspected COVID-19" and underwent testing for SARS-CoV-2 were eligible for inclusion. Testing criteria guided by various health jurisdictions and evolved throughout the project	SARS-CoV-2 RT-PCR test (nasopharyngeal swab)
Peyrony 2020	COVID-19	391	58%	France	ED	Patients tested at ED, decision to test based on clinician's discretion	RT-PCR on nasal swabs
Pivetta 2020	COVID-19	228	47%	Italy	ED	All adults (≥18 years) who screened positive for acute symptoms associated with SARS-CoV-2 infection at triage (= fever, dyspnoea, new or worsening cough, sore throat, diarrhoea, ageusia, anosmia and asthenia)	RT-PCR (nasopharyngeal swabs), and in some cases other information including clinical, lab, imaging
Pokorska-Śpiewak 2021	COVID-19	319	5%	Poland	Mixed in/outpatient paediatric setting	All consecutive paediatric patients referred to a tertiary healthcare department (referral based on clinical symptoms (WHO definition) of the disease or positive epidemiological history (international travel or contact with infected person)	RT-PCR (nasopharyngeal swabs)

Table 2. Study characteristics (cross-sectional prospective studies only) *(Continued)*

Porto 2021	COVID-19	1297	32%	Brazil	Outpatient setting	All patients presenting at the Piquet Carneiro Polyclinic, test indication not specified, but high proportion of symptomatic individuals in recruited population	RT-PCR (nasopharyngeal swabs)
Romero-Gameros 2020	COVID-19	139	52%	Mexico	ED	Patients who sought a respiratory triage assessment at ED of tertiary care hospital due to COVID-19 suspicion	RT-PCR (nasopharyngeal swabs)
Romero-Gameros 2021	COVID-19	2137	54%	Mexico	ED	Adults > 17 years, with high clinical probability of SARS-CoV-2 and confirmatory RT-PCR available	RT-PCR (nasopharyngeal swabs)
Rutten 2020a	COVID-19	1969	44%	The Netherlands	Nursing home	Patients with at least 2 of the following symptoms: fever/feverish feeling, cough and shortness of breath - later on (from 10 April 2020) patients with atypical symptoms were added	RT-PCR test (specimen not specified)
Rutten 2020b	COVID-19	4007	38%	The Netherlands	Nursing home	All nursing home residents with a clinical suspicion of COVID-19 based on the physician's assessment and for whom they had the result of the RT-PCR	RT-PCR test (specimen not specified)
Saegerman 2021	COVID-19	2152	27%	Belgium	ED	All suspected patients directed to the triage centres of 2 university hospital EDs (no definition of 'suspected')	RT-PCR test (specimen not specified)
Salmon Ceron 2020	COVID-19	1824	47%	France	Outpatient setting	Patients suspected of SARS-CoV-2 infection, tested at screening centre	RT-PCR test (nasopharyngeal swabs)
Trubiano 2020	COVID-19	2935	4%	Australia	Outpatient setting	Patients presenting at a COVID-19 rapid assessment screening clinic, meeting DHHS screening criteria[a]	RT-PCR test (nasopharyngeal swabs)
Tudrej 2020	COVID-19	816	24%	France	Primary care/ outpatient setting	Patients referred by GPs for PCR testing at lab	RT-PCR test (nasopharyngeal swabs)
Van Loon 2021	COVID-19	373	50%	Belgium	Outpatient setting	All hospital HCWs self-reporting mild symptoms of an acute upper or lower respirato-	RT-PCR test (nasopharyngeal swab)

Table 2. Study characteristics (cross-sectional prospective studies only) *(Continued)*

						ry tract infection were tested in a large non-academic hospital	
Van Walraven 2021	COVID-19	9172	6%	Canada	Outpatient setting	Presence of symptoms including rhinorrhoea; fever symptoms including rigor, chills, perceived fever, or documented fever at home or at the screening clinic; cough; and shortness of breath. Any infection risk factor including close contact with a person with known or presumed COVID-19 disease or recent travel outside of Canada. In the absence of these indications, HCWs were included if they had symptoms of sore throat, sputum production, or rhinorrhoea.	RT-PCR test (nasopharyngeal and throat swabs)
Villerabel 2021	COVID-19	809	7%	France	Outpatient setting	All HCWs and adult patients presenting themselves at the COVID-19 screening facility of the university hospital of Montpellier	RT-PCR test (nasopharyngeal swabs)
Wee 2020	COVID-19	870	18%	Singapore	ED	Patients presenting with respiratory symptoms or travel history	RT-PCR test (nasopharyngeal swabs)
Wernhart 2020	COVID-19	80	6%	Germany	Primary care	All patients with respiratory symptoms reporting to 3 rural GP offices in North Rhine-Westphalia, Germany	RT-PCR test (nasopharyngeal swabs)
Yonker 2020	COVID-19	174	28%	USA	Mixed in/outpatient paediatric setting	Paediatric patients ≤ 22 years of age; symptoms concerning for COVID-19 or admitted for acute symptoms related to COVID-19 or multisystem inflammatory syndrome in children	RT-PCR test (nasopharyngeal or oropharyngeal swabs)

CT: computed tomography; **ED:** emergency department; **GP:** general practitioner; **HCW:** healthcare worker; **MPOCT:** molecular point-of-care test; **RT-PCR:** reverse transcription polymerase chain reaction; **WHO:** World Health Organization

[a]DHHS (Victorian Department of Health and Human Services) criteria for SARS-CoV-2 testing: fever OR chills in the absence of an alternative diagnosis that explains the clinical presentation OR acute respiratory infection symptoms (e.g. cough, sore throat, shortness of breath, runny nose, loss of smell or loss of taste)

Table 3. Summary estimates of test accuracy for selected index tests, including 95% confidence intervals (bivariate meta-analysis of prospective studies with low risk of bias for participant selection)

Index test	Number of studies	Number of COVID-19 positives/ Total number of participants (%)	Summary sensitivity % (95% CI)	Summary specificity % (95% CI)	Summary LR+ (95% CI)	Summary LR- (95% CI)
Fever	12	3221/28,495 (11.3)	37.6 (23.4 to 54.3)	75.2 (56.3 to 87.8)	1.520 (1.099 to 2.101)	0.829 (0.740 to 0.928)
Dyspnoea	12	2753/19,545 (14.1)	23.3 (16.4 to 31.9)	75.7 (65.2 to 83.9)	0.959 (0.830 to 1.107)	1.013 (0.966 to 1.063)
Cough	11	2586/18,702 (13.8)	62.4 (50.6 to 72.9)	45.4 (33.5 to 57.9)	1.143 (1.043 to 1.253)	0.828 (0.738 to 0.928)
Diarrhoea	11	1633/13,669 (11.9)	18.5 (15.7 to 21.6)	84.1 (79.4 to 87.9)	1.167 (0.967 to 1.408)	0.969 (0.935 to 1.003)
Sore throat	10	2116/14,548 (14.5)	31.0 (20.2 to 44.5)	61.9 (46.7 to 75.0)	0.814 (0.714 to 0.929)	1.114 (1.021 to 1.216)
Fatigue	8	1286/7967 (16.1)	40.2 (19.4 to 65.1)	73.6 (48.4 to 89.3)	1.522 (1.213 to 1.909)	0.813 (0.709 to 0.932)
Rhinorrhoea	7	1620/17,972 (9.0)	30.3 (18.7 to 45.1)	70.0 (56.8 to 80.6)	1.011 (0.848 to 1.205)	0.985 (0.922 to 1.074)
Headache	7	929/10,899 (8.5)	35.8 (17.2 to 60.0)	73.0 (53.4 to 86.4)	1.325 (1.161 to 1.513)	0.879 (0.767 to 1.008)
Anosmia	7	938/9456 (9.9)	26.4 (13.8 to 44.6)	94.2 (90.6 to 96.5)	4.546 (3.461 to 5.972)	0.781 (0.648 to 0.942)
Anosmia or ageusia	6	794/6142 (12.9)	39.2 (26.5 to 53.6)	92.1 (84.5 to 96.2)	4.992 (3.215 to 7.751)	0.659 (0.551 to 0.790)
Myalgia	6	563/2684 (21.0)	37.5 (20.6 to 58.1)	75.4 (58.4 to 87.0)	1.525 (1.207 to 1.926)	0.829 (0.708 to 0.970)
Chills/shivers	5	1080/14,472 (7.5)	25.3 (15.1 to 39.3)	85.0 (72.1 to 92.6)	1.691 (1.231 to 2.323)	0.878 (0.812 to 0.950)
Ageusia	5	748/8644 (8.7)	23.2 (10.6 to 43.3)	92.6 (83.1 to 97.0)	3.137 (1.786 to 5.510)	0.830 (0.701 to 0.982)

Table 3. Summary estimates of test accuracy for selected index tests, including 95% confidence intervals (bivariate meta-analysis of prospective studies with low risk of bias for participant selection) *(Continued)*

CI: confidence interval; **LR+:** positive likelihood ratio; **LR-:** negative likelihood ratio

APPENDICES

Appendix 1. World Health Organization case definitions

Severe pneumonia

Adolescent or adult: fever or suspected respiratory infection, plus one of the following: respiratory rate higher than 30 breaths per minute; severe respiratory distress; or oxygen saturation (SpO_2) 93% or less on room air. Child with cough or difficulty in breathing, plus at least one of the following: central cyanosis or SpO_2 less than 90%; severe respiratory distress (for example, grunting, very severe chest indrawing); signs of pneumonia with a general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions.

Other signs of pneumonia may be present: chest indrawing, fast breathing (in breaths per minute): aged under 2 months: 60 or higher; aged 2 to 11 months: 50 or higher; aged 1 to 5 years: 40 or higher. While the diagnosis is made on clinical grounds; chest imaging may identify or exclude some pulmonary complications.

Acute respiratory distress syndrome (ARDS)

Onset within one week of a known clinical insult or new or worsening respiratory symptoms.

Chest imaging (that is, X-ray, computed tomography (CT) scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules.

Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (for example, echocardiography) to exclude hydrostatic cause of infiltrates/oedema if no risk factor present.

Oxygenation impairment in adults:

- mild ARDS: 200 mmHg less than ratio of arterial oxygen partial pressure/fractional inspired oxygen (PaO_2/FiO_2) 300 mmHg or less (with positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) 5 cmH_2O, or more, or non-ventilated);
- moderate ARDS: 100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg (with PEEP ≥ 5 cmH_2O, or non-ventilated);
- severe ARDS: PaO_2/FiO_2 ≤ 100 mmHg (with PEEP ≥ 5 cm H_2O, or non-ventilated);
- when PaO_2 is not available, SpO_2/FiO_2 ≤ 315 mmHg suggests ARDS (including in non-ventilated patients).

Oxygenation impairment in children: note OI = Oxygenation Index and OSI = Oxygenation Index using SpO_2 . Use PaO_2-based metric when available. If PaO_2 not available, wean FiO_2 to maintain SpO_2 ≤ 97% to calculate OSI or SpO_2/FiO_2 ratio:

- bilevel (non-invasive ventilation or CPAP) ≥ 5 cm H_2O via full-face mask: PaO_2/FiO_2 ≤ 300 mmHg or SpO_2/FiO_2 ≤ 264;
- mild ARDS (invasively ventilated): 4 ≤ OI < 8 or 5 ≤ OSI < 7.5;
- moderate ARDS (invasively ventilated): 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3;
- severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥ 12.3.

Appendix 2. University of Bern living search database

From 30 October 2020

Embase:

(exp SARS-related coronavirus/ or severe acute respiratory syndrome/ or coronavirus disease 2019/ or (coronavir* or corona virus* or HCoV* or ncov* or 2019 cov or covid or covid19 or sars-cov* or sarscov* or sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus* or nCoV).mp.) and 20191101:20301231.(dc).

MEDLINE:

("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "COVID-19" [Supplementary Concept] OR "coronavirus" OR "corona virus" OR "HCoV" OR "nCoV" OR "2019 CoV" OR "covid" OR "covid19" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "SARS-CoV2" OR "SARS-CoV 2" OR "SARS Coronavirus 2") AND (2019/11/01:3000/12/31[PDAT])

Appendix 3. Search classification model

We needed a more efficient approach to keep up with the rapidly increasing volume of COVID-19 literature. A classification model for this specific review was built with the model-building function within Eppi Reviewer, which uses the standard SGCClassifier in Scikit-learn on word trigrams. As outputs, new documents receive a percentage (from the predict_proba function) where scores close to 100 indicate a high probability of belonging to the class 'relevant document' and scores close to 0 indicate a low probability of belonging to the class 'relevant document'. We used three iterations of manual screening (title and abstract screening, followed by full-text review) to build and test classifiers. The final included studies were used as relevant documents, while the remainder of the COVID-19 studies were used as irrelevant documents. The classifier was trained on the first round of selected articles, and tested and retrained on the second round of selected articles. Testing on the second round of selected articles revealed poor positive predictive value but 100% sensitivity at a cut-off of 10. The poor positive predictive value is mainly due to the broad scope of our topic (any signs or symptoms associated with COVID-19)), poor reporting in abstracts, and a small set of included documents.

WHAT'S NEW

Date	Event	Description
15 February 2022	New citation required and conclusions have changed	Findings from 42 prospective studies involving 52,608 participants included in this second update version indicate that there is currently no evidence to support further testing in all individuals presenting only with upper respiratory symptoms such as sore throat, coryza or rhinorrhoea. Based on currently available data, neither absence nor presence of a single sign or symptom are accurate enough to rule in or rule out COVID-19 disease.
16 November 2021	New search has been performed	Review updated with search until 10 June 2021.

HISTORY

Review first published: Issue 7, 2020

Date	Event	Description
4 March 2021	Amended	Corrected peer reviewer's name in Acknowledgements section
11 February 2021	New citation required and conclusions have changed	Review updated: We retrieved 28 more studies on signs and symptoms in suspected COVID-19 patients, allowing pooling of the data for some features and estimation of summary measures of diagnostic accuracy. Moreover, this update contains new studies on the diagnostic value of olfactory symptoms, and includes a limited number of studies on combinations of symptoms.
8 December 2020	New search has been performed	Review updated
7 July 2020	Amended	Resolution of two figures improved

CONTRIBUTIONS OF AUTHORS

JD, JDi, YT, CD, ML, RS, LH, AVdB, and DE, contributed clinical, methodological and/or technical expertise to drafting the protocol. JD co-ordinated contributions from all co-authors and drafted the protocol. ML drafted the QUADAS-2 criteria. AVdB oversaw the overall progress of this review, participated in the selection process, data extraction, quality appraisal and drafting of the manuscript. TS co-ordinated the review process, analysed the data, drafted the manuscript and participated in the selection, data extraction and quality appraisal. JDo, DW, AT, VL, SJ and SH participated in the data extraction, quality appraisal, interpretation of the findings and commented on the manuscript.

DECLARATIONS OF INTEREST

Thomas Struyf: none known

Jonathan J Deeks: no relevant interests; published eight podcasts, including Talk Evidence (BMJ), More-or-Less (Radio 4), Inside Science (Radio 4), The Newscast (Radio 4). Five opinion pieces in Guardian, unHerd and the BMJ. Numerous television, radio and mainstream media interviews giving substantial coverage of scientific issues related to test evaluation for COVID-19. Presented evidence to the House of Lords Select Committee, and the All Parliamentary Party Investigation on COVID-19. Two invited editorials on COVID-19 for the BMJ; Editor, Cochrane Diagnostic Test Accuracy Review editorial team

Jacqueline Dinnes: no relevant interests; Editor, Cochrane Diagnostic Test Accuracy Review editorial team

Yemisi Takwoingi: no relevant interests; Editor, Cochrane Infectious Diseases; Statistical Editor, Cochrane Bone, Joint and Muscle Trauma; Editor, Cochrane Diagnostic Test Accuracy Review editorial team

Clare Davenport: no relevant interests; Contact Editor for Cochrane Diagnostic Test Accuracy Review editorial team and was not involved in the editorial process for this review

Mariska MG Leeflang: no relevant interests; team member, Cochrane Diagnostic Test Accuracy Review editorial team

René Spijker: none known

Lotty Hooft: no relevant interests; editorial roles with the Cochrane Diagnostic Test Accuracy Review editorial team and Prognosis Methods Group implementation team

Devy Emperador: no relevant interests; employed by FIND with funding from DFID and KFW. FIND is a global non-for profit product development partnership and World Health Organization Diagnostic Collaboration Centre. It is FIND's role to accelerate access to high-quality diagnostic tools for low-resource settings and this is achieved by supporting both research and development, and access activities for a wide range of diseases, including COVID-19. FIND has several clinical research projects to evaluate multiple new diagnostic tests against published Target Product Profiles that have been defined through consensus processes. These studies are for diagnostic products developed by private sector companies who provide access to know-how, equipment/reagents, and contribute through unrestricted donations as per FIND policy and external SAC review

Julie Domen: no relevant interests; works as a general practitioner

Anouk Tans: none known

Stéphanie Janssens: no relevant interests; works as a general practitioner in training in 'De Wijkpraktijk' in Antwerp

Dakshitha Wickramasinghe: none known

Viktor Lannoy: none known

Sebastiaan Horn: no relevant interests; works as a resident general practitioner: Praktijkhuis Baarle, University of Antwerp, Antwerp, Belgium

Ann Van den Bruel: none known

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

As the evidence base evolves over the course of the pandemic, we have made some adjustments to our original approach with the following changes between earlier versions of the review and this second update:

- Clarification regarding inclusion criteria: suspicion of infection was interpreted as: **clinical** suspicion of SARS-CoV-2 infection **based on a symptomatic presentation. At least 50% of the study population had to present with COVID-19 compatible symptoms.**
- Both studies using a retrospective and a prospective data collection were included, but **the main findings of this review were based on the prospective studies only**, as retrospective studies tend to overestimate the diagnostic accuracy of the index tests.
- Preprints that were included in previous versions of the review were now excluded (unless they were published in the meantime), and they were no longer included from this update onwards. Consequently, this second review update does not contain any preprints. Records from preprint archives were no longer evaluated for eligible studies because of an increase in COVID-19 study references from recommended diagnostic test accuracy sources (MEDLINE and Embase). For the baseline review, preprint archives were essential to identify emerging evidence; but for the second update, it was no longer necessary to search these sources.
- Search sources included in the protocol and the previous version of this review, the Cochrane COVID-19 Study Register and the CDC Database of COVID-19 Research Articles, were not included in this version as the single source from the University of Bern living search database proved more efficient to process as it did not involve manual effort to deduplicate.
- We did not set out to identify any ongoing studies for this 2022 review version since the review will no longer be updated in its current form (see Objectives).

INDEX TERMS

Medical Subject Headings (MeSH)

*Ageusia [complications]; Anosmia [diagnosis] [etiology]; Artificial Intelligence; Cough [etiology]; *COVID-19 [diagnosis] [epidemiology]; COVID-19 Testing; Dyspnea; Fatigue [etiology]; Fever [diagnosis] [etiology]; Hospitals; Outpatients; *Pharyngitis; Primary Health Care; Prospective Studies; SARS-CoV-2; Sensitivity and Specificity

MeSH check words

Aged; Child; Humans