National Institute for Health and Care Excellence

Suspected acute respiratory infection in over 16s: assessment at first presentation and initial management

[C] Evidence review for diagnostic accuracy of point-of-care tests for viral versus bacterial infection

NICE guideline NG237
Evidence review underpinning the recommendations and recommendations for research in the NICE guideline

October 2023

This evidence review was developed by NIHR Bristol Evidence Synthesis Group

Contents

1 Diagnostic accuracy of point of care tests for acute respiratory infection

1.1 Review question

What is the diagnostic accuracy of near-patient, rapid tests to distinguish between bacterial and viral infection in suspected acute respiratory infection?

1.1.1 Introduction

Respiratory infections are a common cause of illness in adults. They can be caused by viruses (such as a cold), or bacteria. Infections are often self-limiting and resolve without the need for treatment. However, people with more severe symptoms or those at risk of developing serious disease may require treatment. The treatment required depends on the nature of the infection. At present, healthcare professionals use their clinical expertise to identify those who are more severely unwell and/or at risk of deteriorating, and to determine whether they have a respiratory infection caused by a virus or bacteria. However, this is not always easy to establish. Consequently, many people are given antibiotics (to treat a possible bacterial infection), even if the actual cause of their illness is a virus.

Recently, tests have become available which may help to indicate quickly whether a respiratory infection is caused by a virus or bacteria. These tests are known as “rapid point of care” tests because the samples do not need to be sent to specialist laboratories and can be carried out in a GP surgery or in an emergency department. If these tests are very effective, they may be a useful addition to current care. They may be able to identify people who require antibiotics and distinguish them from people who do not require treatment (or require alternative treatment).

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	People aged 16 years or over with suspected acute respiratory infection, including (but not limited to) the following symptoms: • Cough or shortness of breath • Sore throat • Rhinitis
Index tests	• Symptoms and signs of acute respiratory infection; either individual symptoms/signs, or in combination (as part of a clinical decision tool) • “Host-response” (or “biomarker”) point of care tests (POCTs), including:

	○ CRP ○ Procalcitonin ○ CRP and MxA (FebriDx) ○ TRAIL, IP-10 and CRP (ImmunoXpert/MeMed BV) ○ White cell differential count • Multiplex or single POCTs (with a turnaround time of <45 minutes) for (or including) the following specific organisms: ○ Influenza (A and B) ○ Respiratory syncytial virus (RSV)
Comparator/Reference standard	Any reference standard
Outcomes	Diagnostic accuracy measures • Sensitivity • Specificity • Area under the curve (AUC)
Study type	Diagnostic test accuracy studies

For the full protocol see Appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A.

The principal approach used was an overview of systematic reviews. For this overview, we used a two-stage process to select relevant evidence. Initially, we identified all systematic reviews that addressed a question within the scope of the evidence review. From these, we then selected the most relevant systematic review for each index test, considering the search date and comprehensiveness, and the similarity in scope to this review question.

After completing this overview of reviews, we identified two gaps in the available evidence. No systematic reviews addressed the diagnostic accuracy of white cell differential count to distinguish between bacterial or viral infection. In addition, no systematic reviews considered the diagnostic accuracy of multiplex PCR specific to point of care testing in an emergency/ambulatory/primary care setting. We therefore conducted additional searches for primary diagnostic accuracy studies in these areas.

We assessed the risk of bias in the selected systematic reviews using the ROBIS tool and in the primary studies using QUADAS 2. We extracted meta-analysis results from the systematic reviews. Where possible, bivariate random effects meta-analyses were conducted of the primary studies using the 'metandi' function in STATA. If fewer than four studies were available for any analysis then a univariate meta-analysis was conducted.

If data were not suitable for meta-analysis then we present a narrative synthesis of the available results.

We sought data pertaining to the following subgroups of interest in this overview: setting of study, age of patients, presence of chronic co-morbidity, people who are pregnant/post-partum and different reference standards.

We performed GRADE assessments on all syntheses, both those extracted from systematic reviews and those we undertook ourselves on primary studies.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.3.1 Search methods

Systematic literature searches were undertaken to identify published clinical evidence relevant to the review question. Databases were searched using subject headings, free-text terms and where appropriate, study design filters. Two main sets of searches were conducted, the first to identify systematic reviews of diagnostic test accuracy studies and the second to identify primary studies, where there were gaps in the available evidence. The searches for systematic reviews were conducted in the following databases: Medline, Embase, Cochrane Database of Systematic Reviews (CDSR), NIHR Journals Library and Epistemonikos. The searches for primary studies were conducted in Medline and Embase. A pragmatic search of the International Trials Registers (ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP)) was also conducted but did not yield any relevant results.

No date restrictions were placed on the searches.

The searches were iterative, with the initial search structured around broad, top-level terms for the index tests (rapid point-of-care tests or clinical prediction rules) combined with terms for the target condition or causative agents of respiratory tract infections. Later searches included the addition of relevant host-response biomarkers or named tests (devices), as the retrieval of relevant research evidence evolved.

Details of the search strategies (reviews and primary studies) can be found in Appendix B of the evidence report. Searching for grey literature or unpublished literature was not undertaken.

1.1.4 Diagnostic evidence

1.1.4.1 Included systematic reviews

The systematic search carried out to identify potentially relevant systematic reviews found 4450 references (see Appendix B for the literature search strategy).

These 4450 references were screened at title and abstract level against the review protocol, with 4287 excluded at this level. All references were screened separately by two reviewers. Discrepancies were resolved by discussion.

The full texts of 163 review articles were retrieved for closer inspection. 23 of these studies met the criteria specified in the review protocol (Appendix A). For a summary of the 23 reviews see Appendix C, Relevant systematic reviews.

The full texts of these 23 systematic reviews were assessed, considering their currency (search date), similarity in scope to the review question, and comprehensiveness (the number of included studies of relevance to this question). For each index test we selected the most comprehensive review as the primary source of data to answer the review question. Six relevant systematic reviews were identified as being most aligned with the scope of this overview. Details of these reviews are reported in Appendix D, Evidence table 1: Included systematic reviews.

In relation to our planned subgroups, we identified some data presented according to the setting of the study (primary care, emergency care or outpatient settings), and a small amount of data relating to people with a chronic co-morbidity (chronic obstructive pulmonary disease). However, we did not identify any additional information on the subgroups of interest in this review.

The clinical evidence study selection is presented as a PRISMA diagram in Appendix C.

See section 1.1.14 References – included studies for the full references of the included studies.

1.1.4.2 Included primary studies

White cell differential count

A systematic search carried out to identify potentially relevant primary studies on white cell differential count found 455 references (see Appendix B for the literature search strategy).

These 455 references were screened at title and abstract level against the review protocol, with 407 excluded at this level. All references were screened separately by two reviewers. Discrepancies were resolved by discussion.

The full texts of 48 studies were retrieved for closer inspection. 4 of these studies met the criteria specified in the review protocol (Appendix A). For a summary of these 4 studies see Evidence table 2: White cell differential count, primary studies.

See section 1.1.14 References – included studies for the full references of the included studies.

Multiplex PCR tests

A systematic search carried out to identify potentially relevant primary studies on multiplex PCR tests found 587 references (see appendix B for the literature search strategy).

These 587 references were screened at title and abstract level against the review protocol, with 457 excluded at this level. All references were screened separately by two reviewers. Discrepancies were resolved by discussion.

The full texts of 130 studies were retrieved for closer inspection. 12 of these studies met the criteria specified in the review protocol (appendix A). For a summary of these 12 studies see Evidence table 3: Multiplex tests, primary studies.

1.1.4.3 Excluded studies

Details of all reviews and primary studies excluded at full text, along with the main reason for exclusion are given in appendix J.

1.1.5 Summary of studies included in the diagnostic evidence

Table 2 Summary of systematic reviews included in the diagnostic evidence

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias (ROBIS)
Carlton 2021	Adults and children presenting with symptoms of acute respiratory tract infection.	• TRAIL, IP-10 and CRP (ImmunoXpert) • CRP and MxA (FebriDx) • CRP and neopterin	Any reference standard, including consensus of an expert panel, clinical algorithms and microbiology.	• Bacterial respiratory tract infection • Viral respiratory tract infection	Low risk of bias
Gentilotti 2022	Adults and children with symptoms of acute respiratory infection, presenting to primary/emergency care settings.	• Individual symptoms and signs • CRP • Procalcitonin • Various POC tests for influenza	Any reference standard, including chest X-ray, microbiological assessment, expert opinion.	• Bacterial pneumonia • Influenza	Low risk of bias
Minnaard 2017	Adults with suspected lower respiratory tract infection, presenting to primary/emergency care settings.	Clinical prediction models incorporating combinations of symptoms and signs plus CRP measurement	Chest X-ray	• Pneumonia	Low risk of bias
Onwuchekwa 2023	Adults and children. No information on clinical presentation.	Any tests for RSV	RT PCR	• RSV	Low risk of bias
Pazmany 2021	Adults with COPD, presenting with an acute exacerbation to primary care/emergency department or in hospital.	Presence of purulent sputum	Microbiological culture	• Bacterial exacerbation of COPD	Low risk of bias
Schierenberg 2017	Adults with an acute or worsened cough or lower respiratory tract infection,	Combinations of symptoms and signs (clinical prediction models)	Chest X-ray, CT or MRI	• Pneumonia	Low risk of bias

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias (ROBIS)
	present to primary or emergency care.				

COPD chronic obstructive pulmonary disease; CRP C reactive protein; CT computed tomography; IP-10 interferon-γ-induced protein-10; MRI magnetic resonance imaging; MxA myxovirus resistance protein A; POC point of care; RSV respiratory syncytial virus; RT PCR real time polymerase chain reaction; TRAIL TNF-related apoptosis-induced ligand

Table 3 Summary of primary studies included in the diagnostic evidence for white cell differential count

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias (QUADAS 2)
Castro-Guardiola 2000	Adults (n = 284) with suspected pneumonia in an emergency department	• White blood cell count	Chest X-ray, plus clinical symptoms and signs	• Pneumonia	*Risk of bias:* Patient selection: low risk Index test: low risk Reference standard: high risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: high concern Reference standard: low concern
Gulich 1999	Adults (n = 179) with sore throat, presenting to primary care	• White blood cell count	Microbiological culture	• Bacterial pharyngitis	*Risk of bias:* Patient selection: low risk Index test: low risk Reference standard: low risk

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias (QUADAS 2)
					Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: high concern Reference standard: low concern
Holm 2007	Adults (n = 364) with symptoms of a lower respiratory tract infection, presenting to primary care	• White blood cell count	Chest X-ray	• Pneumonia	*Risk of bias:* Patient selection: high risk Index test: high risk Reference standard: low risk Flow and timing: high risk *Applicability:* Patient selection: low concern Index tests: high concern Reference standard: low concern
Liu 2013	Adults (n = 500) with a diagnosis of community acquired pneumonia in an outpatient clinic	• White blood cell count	Microbiological culture and PCR	• Bacterial pneumonia	*Risk of bias:* Patient selection: unclear risk Index test: unclear risk Reference standard: low risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: high concern

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias (QUADAS 2)
					Reference standard: low concern

Table 4 Summary of primary studies included in the diagnostic evidence for multiplex PCR tests

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias
Boku 2013	Adults with acute respiratory infection or fever and contact with influence in a hospital outpatient setting	• Verigene system RV+	Viral culture plus laboratory PCR	• Flu A/B	*Risk of bias:* Patient selection: unclear risk Index test: low risk Reference standard: unclear risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: low concern Reference standard: low concern
Escarate 2022	Adults aged ≥65 years with symptoms of respiratory illness in a care home setting	• Xpert Xpress Flu/RSV	Laboratory PCR	• Flu A • Flu B • RSV	*Risk of bias:* Patient selection: unclear risk Index test: low risk Reference standard: low risk Flow and timing: high risk *Applicability:*

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias
					Patient selection: high concern Index tests: low concern Reference standard: low concern
Farfour 2022	Adults with suspected viral respiratory infection in an emergency department	• Idylla SARS CoV/Flu/RSV	Laboratory PCR	• Flu A • RSV	*Risk of bias:* Patient selection: low risk Index test: unclear risk Reference standard: low risk Flow and timing: high risk *Applicability:* Patient selection: low concern Index tests: low concern Reference standard: low concern
Hansen 2018	Adults (80%) and children (20%) with at least one sign of influenza in an emergency department setting	• Cobas Liat Influenza A/B	Laboratory PCR	• Flu A/B	*Risk of bias:* Patient selection: high risk Index test: low risk Reference standard: low risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: low concern Reference standard: low concern

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias
Maignan 2016	Adults with fever and at least one sign of a respiratory infection in an emergency department setting	• Cobas Liat Influenza A/B	Laboratory PCR	• Flu A • Flu B • Flu A/B	*Risk of bias:* Patient selection: low risk Index test: low risk Reference standard: low risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: low concern Reference standard: low concern
Morris 2021	Adults (and children – subgroup data for adults were used) with symptoms of acute respiratory infection, presenting to the emergency department	• Xpert Xpress Flu/RSV	Laboratory PCR	• Flu A • RSV	*Risk of bias:* Patient selection: high risk Index test: low risk Reference standard: low risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: low concern Reference standard: low concern
Peretz 2020	Adults with suspected influenza in an emergency department	• Xpert Xpress Flu A/B • Simplex Flu A/B and RSV	Rapid antigen test	• Flu A/B	*Risk of bias:* Patient selection: unclear risk Index test: unclear risk Reference standard: high risk

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias
					Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: high concern Reference standard: low concern
Tanei 2014	Adults with symptoms of acute respiratory infection and a fever ≥37ºC	• Verigene RV+	Rapid antigen test	• Flu A/B	*Risk of bias:* Patient selection: low risk Index test: unclear risk Reference standard: high risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: high concern Reference standard: low concern
Valentin 2019	Adults with acute, febrile respiratory tract infection with at least one risk factor for complications of influenza.	• Xpert Xpress Flu/RSV • Cobas Liat Flu A/B	Laboratory based PCR	• Flu A • Flu B • Flu A/B	*Risk of bias:* Patient selection: low risk Index test: low risk Reference standard: low risk Flow and timing: high risk *Applicability:* Patient selection: low concern Index tests: high concern

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias
					Reference standard: low concern
Yin 2022	Adults (77%) and children (23%) with symptoms of acute respiratory infection in an emergency department.	• Cobas Liat Flu A/B	Rapid antigen test plus culture plus Cobas Liat test	• Flu A • Flu B • RSV	*Risk of bias:* Patient selection: unclear risk Index test: low risk Reference standard: high risk Flow and timing: low risk *Applicability:* Patient selection: low concern Index tests: high concern Reference standard: low concern
Youngs 2019	Adults with suspected influenza in an emergency department	• Cobas Liat Flu A/B	Laboratory PCR and alternative rapid multiplex test	• Flu A • Flu B • Flu A/B	*Risk of bias:* Patient selection: low risk Index test: low risk Reference standard: high risk Flow and timing: high risk *Applicability:* Patient selection: low concern Index tests: low concern Reference standard: low concern
Zuurbier 2022	Adults with symptoms of acute respiratory tract infection at home or	• Xpert Xpress Flu/RSV	Laboratory PCR	• RSV	*Risk of bias:* Patient selection: low risk Index test: low risk

Study details	Population	Index test(s)	Reference standard(s)	Target condition(s)	Risk of bias
	in a primary care setting				Reference standard: low risk Flow and timing: high risk *Applicability:* Patient selection: high concern Index tests: low concern Reference standard: low concern

See appendix D for full evidence tables.

1.1.6 Summary of the diagnostic evidence

Summary GRADE tables are reported here for different index tests assessed as part of this review.

Note that, for some outcomes, imprecision was not able to be assessed as the source systematic review did not present any information on heterogeneity. This may result in spuriously high GRADE ratings (as the certainty of the evidence has not been reduced due to this GRADE domain). In addition, for some outcomes we were only able to assess risk of bias across the body of evidence used in the review – not for the specific studies included in an individual meta-analysis. Therefore, all GRADE ratings based on evidence from published systematic reviews are subject to some limitations, and should be interpreted with caution. Finally, for assessment of imprecision, we have used arbitrary thresholds of ≥90% representing high sensitivity/specificity, and ≥75% representing adequate sensitivity/specificity. The certainty of the evidence was reduced by one level if the confidence intervals crossed one of these thresholds, and by two levels if the confidence intervals crossed both thresholds.

Symptoms and signs for the diagnosis of bacterial pneumonia

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Certainty of the body of evidence	Interpretation of effect
Individual symptoms and signs						
Cough	Gentilotti 2022	13 (8423)	Sensitivity	89.1% (66.4 to 97.1)	VERY LOW[1]	Cough may have adequate sensitivity, but the evidence was uncertain. Many people with bacterial pneumonia may have a cough.
			Specificity	13.4% (2.5 to 48.4)	MODERATE[2]	Cough probably has poor specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will also have a cough.
Sputum production	Gentilotti 2022	7 (6392)	Sensitivity	63.9% (40.5 to 82.1)	LOW[3]	Sputum production may have inadequate sensitivity. Many people with bacterial pneumonia may not have productive sputum.
			Specificity	45.3% (25.9 to 66.3)	MODERATE[2]	Sputum production probably has poor specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will still have productive sputum.
Discoloured sputum	Gentilotti 2022	9 (3014)	Sensitivity	54.0% (39.8 to 67.7)	MODERATE[2]	Discoloured sputum probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have discoloured sputum.

			Specificity	53.0% (39.0 to 66.5)	MODERATE[2]	Discoloured sputum probably has poor specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will have discoloured sputum.
Purulent sputum (to detect bacterial exacerbations in people with COPD)	Pazmany 2021	3 (259)	Sensitivity	71% (42 to 90)	VERY LOW[4]	Purulent sputum may have inadequate sensitivity to detect bacterial exacerbations of COPD, but the evidence was uncertain. Many people with bacterial exacerbations of COPD may not have purulent sputum.
			Specificity	51% (30 to 73)	MODERATE[5]	Purulent sputum probably has poor specificity to detect bacterial exacerbations of COPD. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial exacerbations of COPD will still have productive sputum.
Chest pain	Gentilotti 2022	15 (8161)	Sensitivity	33.9% (21.5 to 49.0)	MODERATE[2]	Chest pain probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have chest pain.
			Specificity	73.0% (61.7 to 81.9)	LOW[3]	Chest pain may have inadequate specificity. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may still have chest pain.
Dyspnoea	Gentilotti 2022	14 (6215)	Sensitivity	62.6% (53.3 to 71.1)	MODERATE[2]	Dyspnoea probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have dyspnoea.
			Specificity	45.5% (32.1 to 59.5)	MODERATE[2]	Dyspnoea probably has inadequate specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will still have dyspnoea.

Sore throat	Gentilotti 2022	5 (1096)	Sensitivity	32.6% (20.2 to 48.0)	MODERATE[2]	Sore throat probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have a sore throat.
			Specificity	45.1% (33.1 to 57.6)	MODERATE[2]	Sore throat probably has inadequate specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will still have a sore throat.
Runny nose	Gentilotti 2022	7 (4630)	Sensitivity	45.3% (37.3 to 53.4)	MODERATE[2]	Runny nose probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have a runny nose.
			Specificity	41.8% (28.1 to 56.8)	MODERATE[2]	Runny nose probably has inadequate specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will still have a runny nose.
Myalgia	Gentilotti 2022	6 (1430)	Sensitivity	41.6% (19.0 to 68.5)	MODERATE[2]	Myalgia probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have myalgia.
			Specificity	61.2% (40.7 to 78.4)	LOW[3]	Myalgia may have inadequate specificity. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may still have myalgia.
Chill	Gentilotti 2022	8 (1933)	Sensitivity	45.7% (31.5 to 60.8)	MODERATE[2]	Chills probably have inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have a chill.
			Specificity	60.2% (48.5 to 70.8)	MODERATE[2]	Chills probably have inadequate specificity. Among people with suspected acute respiratory infection, it is likely that

						many people who do not have bacterial pneumonia will still have chills.
Diarrhoea	Gentilotti 2022	5 (4268)	Sensitivity	10.8% (6.3 to 17.7)	MODERATE[2]	Diarrhoea probably has inadequate sensitivity. It is likely that most people with bacterial pneumonia will not have diarrhoea.
			Specificity	89.5% (75.4 to 95.9)	LOW[3]	Diarrhoea may have adequate specificity. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may not have diarrhoea.
Impaired consciousness	Gentilotti 2022	4 (3208)	Sensitivity	11.7% (9.3 to 14.5)	MODERATE[2]	Impaired consciousness probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have impaired consciousness.
			Specificity	92.9% (90.5 to 94.7)	MODERATE[2]	Impaired consciousness probably has high specificity. Among people with suspected acute respiratory infection, it is likely that most people who do not have bacterial pneumonia will not have impaired consciousness.
$Sp0_2$	Gentilotti 2022	6 (2821)	Sensitivity	22.8% (12.4 to 38.2)	MODERATE[2]	Low oxygen saturations probably have inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have low oxygen saturations.
			Specificity	86.6% (80.7 to 90.9)	LOW[3]	Low oxygen saturations may have adequate specificity. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may not have low oxygen saturations.
Fever >37.8^{0}C	Gentilotti 2022	17 (11219)	Sensitivity	42.0% (26.7 to 58.9)	MODERATE[2]	Fever probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have a fever.

			Specificity	80.4% (59.8 to 91.9)	VERY LOW[1]	Fever may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may also not have a fever.
Systolic BP	Gentilotti 2022	4 (3262)	Sensitivity	9.6% (2.8 to 28.3)	MODERATE[2]	Low systolic blood pressure probably has inadequate sensitivity. It is likely that most people with bacterial pneumonia will not have a low systolic blood pressure.
			Specificity	95.0% (80.7 to 98.8)	LOW[3]	Low systolic blood pressure may have high specificity. Among people with suspected acute respiratory infection, most people who do not have bacterial pneumonia may not have a low systolic blood pressure.
Tachycardia	Gentilotti 2022	11 (9474)	Sensitivity	27.2% (15.1 to 43.9)	MODERATE[2]	Tachycardia probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have tachycardia.
			Specificity	84.2% (71.5 to 91.9)	VERY LOW[1]	Tachycardia may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may not have tachycardia.
Tachypnoea	Gentilotti 2022	12 (10351)	Sensitivity	27.9% (13.1 to 49.8)	MODERATE[2]	Tachypnoea probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have tachypnoea.
			Specificity	80.2% (58.2 to 92.2)	VERY LOW[1]	Tachypnoea may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may not have tachypnoea.

Reduced breath sounds	Gentilotti 2022	4 (459)	Sensitivity	24.7% (8.3 to 54.4)	MODERATE[2]	Reduced breath sounds probably have inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have reduced breath sounds.
			Specificity	89.0% (75.0 to 95.6)	LOW[3]	Reduced breath sounds may have adequate specificity. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may not have reduced breath sounds.
Wheezing	Gentilotti 2022	6 (2403)	Sensitivity	17.3% (9.6 to 29.2)	MODERATE[2]	Wheezing probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have wheeze.
			Specificity	86.4% (70.5 to 94.4)	VERY LOW[1]	Wheezing may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may not have wheeze.
Crackles	Gentilotti 2022	10 (6175)	Sensitivity	40.3% (23.6 to 59.7)	MODERATE[2]	Presence of crackles on auscultation probably have inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have crackles.
			Specificity	83.1% (58.5 to 94.5)	VERY LOW[1]	Presence of crackles on auscultation may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may not have crackles.
Combinations of symptoms and signs						
Presence/absence of specific symptoms and signs	Schierenberg 2017	6 (not reported)	Area under the curve	Ranged from 53% to 79% depending on model used	VERY LOW[6]	Combinations of signs and symptoms may not have adequate diagnostic accuracy to identify bacterial

						pneumonia, although this will vary according to the model used.
Combinations of symptoms and signs plus CRP measurement						
Predicted risk threshold 2.5%	Minnaard 2017	8 (5308)	Sensitivity	97% (95 to 98)	MODERATE[7]	At a predicted risk threshold of 2.5%, clinical prediction models incorporating CRP probably have adequate sensitivity. It is likely that most people with bacterial pneumonia will have a predicted risk of >2.5%. .
			Specificity	36% (34 to 37)	MODERATE[7]	At a predicted risk threshold of 2.5%, clinical prediction models incorporating CRP probably have inadequate specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will also have a predicted risk >2.5%.
Predicted risk threshold 20%	Minnaard 2017	8 (5308)	Sensitivity	70% (66 to 73)	MODERATE[7]	At a predicted risk threshold of 20%, clinical prediction models incorporating CRP probably have inadequate sensitivity. It is likely that many people with bacterial pneumonia will have a predicted risk <20%.
			Specificity	90% (89 to 91)	LOW[8]	At a predicted risk threshold of 20%, clinical prediction models incorporating CRP may have high specificity. Among people with suspected acute respiratory infection, most people who do not have bacterial pneumonia may have a predicted risk <20%.

1 Downgraded by three levels due to a serious risk of bias and very serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

2 Downgraded by one level for a serious risk of bias. Note that inconsistency was not able to be assessed for this outcome.

3 Downgraded by two levels due to a serious risk of bias and serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

4 Downgraded by three levels for a serious risk of bias and very serious imprecision.

5 Downgraded by one level for a serious risk of bias.

6 Downgraded by one level for serious inconsistency, one level for serious imprecision and one level for publication bias, as authors were unable to access data from at least four publications for inclusion in their IPD meta-analysis.

7 Downgraded by one level for publication bias, as authors were unable to access data from at least four publications for inclusion in their IPD meta-analysis.

8 Downgraded by one level for publication bias (as authors were unable to access data from at least four publications for inclusion in their IPD meta-analysis) and downgraded by one level for serious imprecision.

Host biomarkers to detect bacterial or viral respiratory tract infection

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Certainty of the body of evidence	Interpretation of effect
CRP						
CRP >10mg/L	Gentilotti 2022	4 (944)	Sensitivity	92% (56 to 99)	VERY LOW[1]	CRP (>10mg/L) may have high sensitivity, but the evidence was uncertain. Most people with bacterial pneumonia may have a CRP level >10mg/L.
			Specificity	43% (22 to 66)	MODERATE[2]	CRP (>10mg/L) probably has inadequate specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will have a CRP level >10mg/L.

CRP >20mg/L	Gentilotti 2022	5 (3531)	Sensitivity	83% (64 to 93)	VERY LOW[1]	CRP (>20mg/L) may have adequate sensitivity, but the evidence was uncertain. Many people with bacterial pneumonia may have a CRP level >20mg/L.
			Specificity	55% (37 to 73)	MODERATE[2]	CRP (>20mg/L) probably has inadequate specificity. Among people with suspected acute respiratory infection, it is likely that many people who do not have bacterial pneumonia will have a CRP level >20mg/L.
CRP >20mg/L (primary care only, adults and children)	Gentilotti 2022	4 (3362)	Sensitivity	78% (57 to 90)	VERY LOW[3]	CRP (>20mg/L) may have adequate sensitivity in a primary care setting, but the evidence was uncertain. Many people with bacterial pneumonia may have a CRP level >20mg/L.
			Specificity	58% (36 to 78)	VERY LOW[4]	CRP (>20mg/L) probably has inadequate specificity in a primary care setting. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may have a CRP level >20mg/L. .
CRP >50mg/L	Gentilotti 2022	5 (4219)	Sensitivity	77% (51 to 91)	VERY LOW[1]	CRP (>50mg/L) may have adequate sensitivity, but the evidence was uncertain. Many people with bacterial pneumonia may have a CRP level >50mg/L
			Specificity	74% (51 to 88)	LOW[5]	CRP (>50mg/L) may have inadequate specificity. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may have a CRP level >50mg/L.
CRP >100mg/L	Gentilotti 2022	6 (4418)	Sensitivity	52% (31 to 72)	MODERATE[2]	CRP (>100mg/L) probably has inadequate sensitivity. It is likely that many people with bacterial pneumonia will not have a CRP level >100mg/L
			Specificity	91% (79 to 97)	LOW[5]	CRP (>100mg/L) may have high specificity. Among people with suspected acute respiratory infection, most people

						who do not have bacterial pneumonia may have a CRP level ≤100mg/L.
Procalcitonin						
Procalcitonin >0.1 mcg/mL	Gentilotti 2022	4 (1092)	Sensitivity	74% (38 to 93)	VERY LOW[1]	Procalcitonin (>0.1mcg/mL) may have inadequate sensitivity, but the evidence was very uncertain. Many people with bacterial pneumonia may not have a procalcitonin level >0.1mcg/mL.
			Specificity	74% (36 to 94)	VERY LOW[1]	Procalcitonin (>0.1mcg/mL) may have inadequate specificity, but the evidence was very uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may have a procalcitonin level >0.1mcg/mL.
Procalcitonin >0.25 mcg/mL	Gentilotti 2022	5 (4019)	Sensitivity	44% (14 to 79)	LOW[5]	Procalcitonin (>0.25mcg/mL) may have inadequate sensitivity. Many people with bacterial pneumonia may not have a procalcitonin level >0.25mcg/mL.
			Specificity	89% (50 to 98)	VERY LOW[1]	Procalcitonin (>0.25mcg/mL) may have adequate specificity. Among people with suspected acute respiratory infection, most people who do not have bacterial pneumonia may have a procalcitonin level ≤0.25mcg/mL.
Procalcitonin >0.50 mcg/mL (adults and children)	Gentilotti 2022	4 (1195)	Sensitivity	44% (19 to 33)	LOW[6]	Procalcitonin (>0.50mcg/mL) may have inadequate sensitivity. Many people with bacterial pneumonia may not have a procalcitonin level >0.50mcg/mL.
			Specificity	93% (43 to 100)	VERY LOW[3]	Procalcitonin (>0.50mcg/mL) may have high specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, most people who do not have bacterial pneumonia may have a procalcitonin level ≤0.50mcg/mL.

TRAIL, IP-10 and CRP (ImmunoXpert)						
TRAIL, IP-10 and CRP to diagnose bacterial infection (adults and children)	Carlton 2021	4 (1291)	Sensitivity	85% (75 to 91)	VERY LOW[7]	ImmunoXpert may have adequate sensitivity, but the evidence was uncertain. Most people with bacterial pneumonia may have a positive (bacterial) result.
			Specificity	86% (73 to 93)	VERY LOW[8]	ImmunoXpert may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia may have a negative (bacterial) result.
TRAIL, IP-10 and CRP to diagnose viral infection (adults and children)	Carlton 2021	3 (989)	Sensitivity	90% (79 to 96)	VERY LOW[9]	ImmunoXpert may have high sensitivity, but the evidence was uncertain. Most people with viral infection may have a positive (viral) result.
			Specificity	92% (83 to 96)	VERY LOW[7]	ImmunoXpert may have high specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have a viral infection may have a negative (viral) result.
CRP and MxA (FebriDx)						
CRP and MxA to diagnose bacterial infection (adults and children)	Carlton 2021	4 (598)	Sensitivity	84% (75 to 90)	LOW[10]	FebriDx may have adequate sensitivity. Many people with bacterial pneumonia may have a positive (bacterial) result.
			Specificity	93% (90 to 95)	MODERATE[11]	FebriDx probably has high specificity. Among people with suspected acute respiratory infection, it is likely that most people who do not have bacterial pneumonia will have a negative (bacterial) result.
CRP and MxA to diagnose viral infection	Carlton 2021	4 (583)	Sensitivity	87% (72 to 95)	VERY LOW[12]	FebriDx may have adequate sensitivity, but the evidence was uncertain. Many people with viral infection may have a positive (viral) result.

(adults and children)			Specificity	82% (66 to 86)	LOW[10]	FebriDx may have adequate specificity. Among people with suspected acute respiratory infection, many people who do not have a viral infection may have a negative (viral) result.
White cell differential count						
White cell count to diagnose pneumonia	Castro-Guardiola 2000, Holm 2007, Liu 2013	3 (1148)	2 studies reported sensitivity estimates ranging from 10.1 to 71.1%, and specificity estimates ranging from 31.3 to 94.6%, depending on the threshold used. 1 study reported an area under the curve of 0.65.		VERY LOW[13]	The evidence regarding the diagnostic accuracy of white cell counts to diagnose bacterial respiratory infection was very uncertain.
White cell count to diagnose bacterial pharyngitis	Gulich 1999	1 (179)	Area under the curve	0.68 (no confidence intervals)	LOW[14]	White cell count may have inadequate diagnostic accuracy to diagnose bacterial pharyngitis.
Other host biomarkers						
CRP and neopterin to diagnose bacterial infection	Carlton 2021	1 (198)	Sensitivity	80% (71 to 86)	VERY LOW[15]	CRP and neopterin may have adequate sensitivity, but the evidence was uncertain. Many people with bacterial pneumonia may have an elevated CRP/neopterin level.
			Specificity	82% (71 to 89)	VERY LOW[15]	CRP and neopterin may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people who do not have bacterial pneumonia will not have an elevated CRP/neopterin level.

1 Downgraded by one level for serious risk of bias, and by two levels for very serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

2 Downgraded by one level for serious risk of bias. Note that inconsistency was not able to be assessed for this outcome.

3 Downgraded by one level for serious risk of bias, one level for indirectness (as adults and children were included) and by two levels for very serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

4 Downgraded by one level for serious risk of bias, one level for indirectness (as adults and children were included) and by one level for serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

5 Downgraded by one level for serious risk of bias, and by one level for serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

6 Downgraded by one level for serious risk of bias and one level for indirectness (as adults and children were included). Note that inconsistency was not able to be assessed for this outcome.

7 Downgraded by one level for serious risk of bias, one level for indirectness (as adults and children were included) and by one level for serious imprecision.

8 Downgraded by one level for serious risk of bias, one level for indirectness (as adults and children were included) and by two levels for very serious imprecision.

9 Downgraded by one level for serious risk of bias, one level for indirectness (as adults and children were included), one level for inconsistency and by one level for serious imprecision.

10 Downgraded by one level for serious indirectness (as adults and children were included) and one level for serious imprecision.

11 Downgraded by one level for serious indirectness (as adults and children were included).

12 Downgraded by one level for serious indirectness (as adults and children were included) and two levels for very serious imprecision.

13 Downgraded by one level for serious risk of bias, one level for indirectness (as all index tests were carried out in a laboratory setting, not actually at point of care), one level for inconsistency and by two levels for very serious imprecision (only a narrative synthesis was possible, and estimates from individual studies varied considerably).

14 Downgraded by one level for indirectness (as the index test was carried out in a laboratory setting, not actually at point of care) and by one level for serious imprecision (no confidence intervals were reported)

15 Downgraded by one level for serious risk of bias, one level for indirectness (as neopterin tests were carried out in a laboratory setting, not actually at point of care), and by one level for serious imprecision.

Single pathogen tests for influenza and RSV

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Certainty of the body of evidence	Interpretation of effect
Single pathogen tests for influenza						
Immunochromatography	Gentilotti 2022	15 (2897)	Sensitivity	65% (47 to 79)	LOW[1]	Immunochromatography tests may have inadequate sensitivity. Many people with influenza may not have a positive test.
			Specificity	96% (92 to 98)	MODERATE[2]	Immunochromatography tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without influenza will have a negative test.
Immunochromatography (adults and children, primary care only)	Gentilotti 2022	11 (3351)	Sensitivity	56% (36 to 74)	LOW[3]	Immunochromatography tests may have inadequate sensitivity in a primary care setting. Many people with influenza may not have a positive test.
			Specificity	95% (89 to 98)	VERY LOW[4]	Immunochromatography tests may have high specificity in a primary care setting, but the evidence was uncertain. Among people with suspected acute respiratory infection, most people without influenza may have a negative test.
Immunochromatography (adults and children, emergency department only)	Gentilotti 2022	25 (15021)	Sensitivity	71% (60 to 80)	LOW[5]	Immunochromatography tests may have inadequate sensitivity in an emergency department setting. Many people with influenza may not have a positive test.
			Specificity	98% (96 to 99)	MODERATE[6]	Immunochromatography tests probably have high specificity in an emergency department setting. Among

						people with suspected acute respiratory infection, it is likely that most people without influenza will have a negative test.
Immunochromatography (adults and children, outpatient department only)	Gentilotti 2022	17 (6110)	Sensitivity	66% (55 to 76)	LOW[5]	Immunochromatography tests may have inadequate sensitivity in an outpatient setting. Many people with influenza may not have a positive test.
			Specificity	97% (93 to 99)	MODERATE[6]	Immunochromatography tests probably have high specificity in an outpatient setting. Among people with suspected acute respiratory infection, it is likely that most people without influenza will have a negative test.
Direct immunofluorescence (adults and children)	Gentilotti 2022	19 (7635)	Sensitivity	78% (67 to 86)	VERY LOW[4]	Direct immunofluorescence may have adequate sensitivity, but the evidence was very uncertain. Many people with influenza may have a positive test.
			Specificity	95% (90 to 98)	LOW[3]	Direct immunofluorescence tests may have high specificity. Among people with suspected acute respiratory infection, most people without influenza may have a negative test.
Direct immunofluorescence (adults and children, emergency department only)	Gentilotti 2022	5 (1314)	Sensitivity	82% (72 to 89)	VERY LOW[4]	Direct immunofluorescence may have adequate sensitivity in an emergency department setting, but the evidence was very uncertain. Many people with influenza may have a positive test.
			Specificity	96% (93 to 97)	LOW[3]	Direct immunofluorescence tests may have high specificity in an emergency department setting. Among people with suspected acute respiratory infection, most people without influenza may have a negative test.
Optical immunoassay (adults and children)	Gentilotti 2022	9 (3910)	Sensitivity	68% (51 to 81)	VERY LOW[4]	Optical immunoassays may have inadequate sensitivity, but the evidence was very uncertain. Many people with influenza may not have a positive test.

			Specificity	88% (81 to 93)	VERY LOW[4]	Optical immunoassays may have adequate specificity, but the evidence was very uncertain. Among people with suspected acute respiratory infection, many people without influenza may have a negative test.
MariPOC test (adults and children)	Gentilotti 2022	5 (1231)	Sensitivity	78% (61 to 89)	VERY LOW[4]	MariPOC tests may have adequate sensitivity, but the evidence was very uncertain. Many people with influenza may have a positive test.
			Specificity	99% (97 to 99)	LOW[3]	MariPOC tests may have high specificity. Among people with suspected acute respiratory infection, most people without influenza may have a negative test.
Chemiluminescent neuraminidase assay (adults and children)	Gentilotti 2022	4 (787)	Sensitivity	81% (51 to 94)	VERY LOW[7]	Chemiluminescent neuraminidase assays may have adequate sensitivity, but the evidence was uncertain. Many people with influenza may have a positive test.
			Specificity	82% (65 to 91)	VERY LOW[7]	Chemiluminescent neuraminidase assays may have adequate specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, many people without influenza may have a negative test.
Nucleic acid amplification tests: standalone, single pathogen PCR (adults and children)	Gentilotti 2022	30 (25027)	Sensitivity	95.1% (89.3 to 97.8)	VERY LOW[4]	Single pathogen PCR tests may have high sensitivity, but the evidence was uncertain. Most people with influenza may have a positive test.
			Specificity	97.5% (95.5 to 98.7)	LOW[3]	Single pathogen PCR tests may have high specificity. Among people with suspected acute respiratory infection, most people without influenza may have a negative test.
Nucleic acid amplification tests: non-PCR based	Gentilotti 2022	23 (4863)	Sensitivity	92% (88 to 94)	VERY LOW[4]	Non-PCR based nucleic acid amplification tests may have high sensitivity, but the evidence was uncertain. Most people with influenza may have a positive test.

(adults and children)			Specificity	98% (95 to 99)	LOW[3]	Non-PCR based nucleic acid amplification tests may have high specificity. Among people with suspected acute respiratory infection, most people without influenza may have a negative test.
Nucleic acid amplification tests: non-PCR based (adults and children, emergency department only)	Gentilotti 2022	14 (3138)	Sensitivity	91% (87 to 94)	VERY LOW[4]	Non-PCR based nucleic acid amplification tests may have high sensitivity in an emergency department setting, but the evidence was uncertain. Most people with influenza may have a positive test.
			Specificity	98% (95 to 99)	LOW[3]	Non-PCR based nucleic acid amplification tests may have high specificity in an emergency department setting. Among people with suspected acute respiratory infection, most people without influenza may have a negative test.
Single pathogen tests for RSV						
Direct immunofluorescence	Onwuchekwa 2023	1 (49)	Sensitivity	56% (31 to 78)	VERY LOW[8]	Direct immunofluorescence may have inadequate sensitivity, but the evidence was uncertain. Many people who have RSV may not have a positive test.
			Specificity	100% (89 to 100)	VERY LOW[8]	Direct immunofluorescence may have high specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, most people without RSV may have a negative test.
Rapid antigen test	Onwuchekwa 2023	1 (281)	Sensitivity	18% (12 to 27)	LOW[9]	Rapid antigen tests may have inadequate sensitivity. Most people who have RSV may not have a positive test.
			Specificity	98% (86 to 100)	VERY LOW[10]	Rapid antigen tests may have high specificity, but the evidence was uncertain. Among people with suspected acute respiratory infection, most people without RSV may have a negative test.

1 Downgraded by one level for serious risk of bias and one level for serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

2 Downgraded by one level for serious risk of bias. Note that inconsistency was not able to be assessed for this outcome.

3 Downgraded by one level for serious risk of bias and one level for indirectness (as adults and children were included). Note that inconsistency was not able to be assessed for this outcome.

4 Downgraded by one level for serious risk of bias, one level for indirectness (as adults and children were included), and one level for serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

5 Downgraded by one level for serious indirectness and one level for serious imprecision.

6 Downgraded by one level for serious indirectness.

7 Downgraded by one level for serious risk of bias, one level for indirectness (as adults and children were included), and two levels for very serious imprecision. Note that inconsistency was not able to be assessed for this outcome.

8 Downgraded by two levels for imprecision due to wide confidence intervals and very small sample size, and one level for indirectness (as unclear whether this test was suitable for use at point of care).

9 Downgraded by one level for risk of bias and one level for indirectness (as this study included some retrospective [frozen] samples, and may have included hospitalised participants).

10 Downgraded by one level for risk of bias, one level for indirectness (as this study included some retrospective [frozen] samples, and may have included hospitalised participants) and one level for serious imprecision.

Multiplex PCR for diagnosis of influenza and RSV

Index tests	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Certainty of the body of evidence	Interpretation of effect
RSV						

All multiplex PCR tests for RSV	Farfour 2022, Morris 2021, Yin 2022, Youngs 2019, Zuurbier 2022	5 studies (2273)	Sensitivity	84.9% (73.5 to 91.9)	VERY LOW[1]	Multiplex PCR tests may have adequate sensitivity, but the evidence was uncertain. Most people with RSV may have a positive test.
			Specificity	99.5% (99.1 to 99.7)	MODERATE[2]	Multiplex PCR tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without RSV will have a negative test.
Cobas Liat tests for RSV	Yin 2022, Youngs 2019	2 studies (965)	Sensitivity	86.7% (59.5 to 96.6)	VERY LOW[1]	Cobas Liat tests may have adequate sensitivity, but the evidence was uncertain. Most people with RSV may have a positive test.
			Specificity	99.3% (98.5 to 99.6)	MODERATE[2]	Cobas Liat tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without RSV will have a negative test.
Xpert Xpress tests for RSV	Morris 2021, Zuurbier 2022	2 studies (1109)	Sensitivity	84.5% (69.4 to 92.9)	VERY LOW[1]	Xpert Xpress tests may have adequate sensitivity, but the evidence was uncertain. Most people with RSV may have a positive test.
			Specificity	99.6% (99.0 to 99.9)	MODERATE[2]	Xpert Xpress tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without RSV will have a negative test.
Influenza A						
All multiplex PCR tests for influenza A	Escarate 2022,	8 studies (2212)	Sensitivity	98.2% (90.7 to 99.7)	LOW[3]	Multiplex PCR tests may have high sensitivity. Most people with influenza A may have a positive test.

	Farfour 2022, Morris 2021, Maignan 2016, Valentin 2019 (two tests included), Yin 2022, Youngs 2019.		Specificity	98.6% (96.6 to 99.4)	LOW[3]	Multiplex PCR tests may have high specificity. Among people with suspected acute respiratory infection, most people without influenza A may have a negative test.
Cobas Liat tests for influenza A	Maignan 2016, Valentin 2019, Yin 2022, Youngs 2019.	4 studies (1259)	Sensitivity	99.8% (18.8 to 100)	VERY LOW[4]	Cobas Liat tests may have high sensitivity, but the evidence was uncertain. Most people with influenza A may have a positive test.
			Specificity	97.9 (94.0 to 99.3)	MODERATE[5]	Cobas Liat tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without influenza A will have a negative test.
Xpert Xpress tests for influenza A	Escarate 2022, Morris 2021, Valentin 2019.	3 studies (754)	Sensitivity	97.0% (92.9 to 98.7)	MODERATE[2]	Xpert Xpress tests probably have adequate sensitivity. It is likely that most people with influenza A will have a positive test.
			Specificity	98.5% (96.2 to 99.4)	MODERATE[2]	Xpert Xpress tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without influenza A will have a negative test.

Influenza B						
All multiplex PCR tests for influenza B	Escarate 2022, Maignan 2016, Valentin 2019 (two tests included), Yin 2022, Youngs 2019.	6 studies (1823)	Sensitivity	94.5% (88.6 to 97.5)	VERY LOW[6]	Multiplex PCR tests may have high sensitivity, but the evidence was uncertain. Most people with influenza B may have a positive test.
			Specificity	99.1 (98.1 to 99.6)	LOW[3]	Multiplex PCR tests may have high specificity. Among people with suspected acute respiratory infection, most people without influenza B may have a negative test.
Cobas Liat tests for influenza B	Maignan 2016, Valentin 2019, Yin 2022, Youngs 2019.	4 studies (1420)	Sensitivity	92.9% (84.3 to 96.9)	LOW[6]	Cobas Liat tests may have high sensitivity. Most people with influenza B may have a positive test.
			Specificity	99.0% (97.6 to 99.6)	MODERATE[5]	Cobas Liat tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without influenza B will have a negative test.
Xpert Xpress tests for influenza B	Escarate 2022, Valentin 2019.	2 studies (403)	Sensitivity	96.4% (90.7 to 99.0)	MODERATE[2]	Xpert Xpress tests probably have high sensitivity. It is likely that most people with influenza B will have a positive test.
			Specificity	99.4% (97.4 to 99.8)	MODERATE[2]	Xpert Xpress tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without influenza B will have a negative test.

Influenza A and/or B						
All multiplex PCR tests for influenza A/B	Boku 2013, Escarate 2022, Hansen 2018, Maignan 2016, Valentin 2019 (two tests included), Yin 2022, Youngs 2019.	8 studies (2162)	Sensitivity	97.4% (92.9 to 99.0)	LOW[3]	Multiplex PCR tests may have high sensitivity. Most people with influenza A/B may have a positive test.
			Specificity	97.0% (94.5 to 98.4)	LOW[3]	Multiplex PCR tests may have high specificity. Among people with suspected acute respiratory infection, most people without influenza A/B may have a negative test.
Cobas Liat tests for influenza A/B	Hansen 2018, Maignan 2016, Valentin 2019, Yin 2022, Youngs 2019.	5 studies (1712)	Sensitivity	97.1% (88.6 to 99.3)	LOW[6]	Cobas Liat tests may have high sensitivity. Most people with influenza A/B may have a positive test.
			Specificity	96.8% (93.2 to 98.5)	MODERATE[5]	Cobas Liat tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without influenza A/B will have a negative test.
Xpert Xpress tests for influenza A/B	Escarate 2022,	2 studies (403)	Sensitivity	97.5% (93.6 to 99.1)	MODERATE[2]	Xpert Xpress tests probably have high sensitivity. It is likely that most people with influenza A/B will have a positive test.

	Valentin 2019		Specificity	97.5% (94.5 to 98.9)	MODERATE[2]	Xpert Xpress tests probably have high specificity. Among people with suspected acute respiratory infection, it is likely that most people without influenza A/B will have a negative test.

1 Downgraded by one level for serious risk of bias and by two levels for very serious imprecision.

2 Downgraded by one level for serious risk of bias.

3 Downgraded by one level for serious risk of bias and by one level for serious inconsistency (due to a wide prediction region and relatively large tau^2).

4 Downgraded by one level for serious inconsistency (due to a wide prediction region and relatively large tau^2) and by two levels for very serious imprecision.

5 Downgraded by one level for serious inconsistency (due to a wide prediction region and relatively large tau^2).

6 Downgraded by one level for serious inconsistency (due to a wide prediction region and relatively large tau^2) and by one level for serious imprecision.

7 Downgraded by one level for risk of bias, by one level for serious inconsistency (due to a wide prediction region and relatively large tau^2) and by one level for serious imprecision.

See appendix F for full GRADE tables

We excluded two studies (Peretz 2020, Tanei 2014) from the meta-analyses of multiplex tests. Both of these studies assessed the diagnostic accuracy of a rapid antigen test, and used a rapid multiplex PCR test as the reference standard. In theory, these studies could be used to evaluate the sensitivity and specificity of rapid multiplex PCR against the rapid antigen test (which would be eligible according to our liberal inclusion of any reference standard). However, the rapid antigen tests were not considered to be a reference standard by the authors of the primary studies, and we did not consider it appropriate to estimate sensitivity and specificity of the multiplex tests against this test as a reference. We report the percentage positive agreement and percentage negative agreement for multiplex PCR and rapid antigen tests in the full evidence table, although urge caution in their interpretation.

1.1.7 Economic evidence

Economic evidence was not considered in this review. Cost effectiveness is assessed as part of the companion review questions in this guideline.

1.1.14 References – included studies

1.1.14.1 Included systematic reviews

Bruning AHL, Leeflang MMG, Vos JMBW, Spijker R, de Jong MD, Wolthers KC, et al. Rapid Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review and Meta-analysis. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2017;65(6):1026-32.

Carlton HC, Savovic J, Dawson S, Mitchelmore PJ, Elwenspoek MMC. Novel point-of-care biomarker combination tests to differentiate acute bacterial from viral respiratory tract infections to guide antibiotic prescribing: a systematic review. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2021;27(8):1096-108.

Chartrand C, Leeflang MMG, Minion J, Brewer T, Pai M. Accuracy of rapid influenza diagnostic tests: a meta-analysis. Annals of internal medicine. 2012;156(7):500-11.

Chartrand C, Tremblay N, Renaud C, Papenburg J. Diagnostic Accuracy of Rapid Antigen Detection Tests for Respiratory Syncytial Virus Infection: Systematic Review and Meta-analysis. Journal of clinical microbiology. 2015;53(12):3738-49.

Engel MF, Paling FP, Hoepelman AIM, van der Meer V, Oosterheert JJ. Evaluating the evidence for the implementation of C-reactive protein measurement in adult patients with suspected lower respiratory tract infection in primary care: a systematic review. Family practice. 2012;29(4):383-93.

Falk G, Fahey T. C-reactive protein and community-acquired pneumonia in ambulatory care: systematic review of diagnostic accuracy studies. Family practice. 2009;26(1):10-21.

Gentilotti E, De Nardo P, Cremonini E, Gorska A, Mazzaferri F, Canziani LM, et al. Diagnostic accuracy of point-of-care tests in acute community-acquired lower respiratory tract infections. A systematic review and meta-analysis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2022;28(1):13-22.

Hill AT, Gold PM, El Solh AA, Metlay JP, Ireland B, Irwin RS, et al. Adult Outpatients With Acute Cough Due to Suspected Pneumonia or Influenza: CHEST Guideline and Expert Panel Report. Chest. 2019;155(1):155-67.

Han M-Y, Xie T-A, Li J-X, Chen H-J, Yang X-H, Guo X-G. Evaluation of Lateral-Flow Assay for Rapid Detection of Influenza Virus. BioMed research international. 2020;2020:3969868.

Hoult G, Gillespie D, Wilkinson TMA, Thomas M, Francis NA. Biomarkers to guide the use of antibiotics for acute exacerbations of COPD (AECOPD): a systematic review and meta-analysis. BMC pulmonary medicine. 2022;22(1):194.

Htun TP, Sun Y, Chua HL, Pang J. Clinical features for diagnosis of pneumonia among adults in primary care setting: A systematic and meta-review. Scientific reports. 2019;9(1):7600.

Huang HS, Tsai CL, Chang J, Hsu TC, Lin S, Lee CC. Multiplex PCR system for the rapid diagnosis of respiratory virus infection: systematic review and meta-analysis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2018;24(10):1055-63.

Lee J, Song J-U, Kim YH. Diagnostic Accuracy of the Quidel Sofia Rapid Influenza Fluorescent Immunoassay in Patients with Influenza-like Illness: A Systematic Review and Meta-analysis. Tuberculosis and respiratory diseases. 2021;84(3):226-36.

Merckx J, Wali R, Schiller I, Caya C, Gore GC, Chartrand C, et al. Diagnostic Accuracy of Novel and Traditional Rapid Tests for Influenza Infection Compared With Reverse Transcriptase Polymerase Chain Reaction: A Systematic Review and Meta-analysis. Annals of internal medicine. 2017;167(6):394-409.

Minnaard MC, de Groot JAH, Hopstaken RM, Schierenberg A, de Wit NJ, Reitsma JB, et al. The added value of C-reactive protein measurement in diagnosing pneumonia in primary care: a meta-analysis of individual patient data. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2017;189(2):E56-E63.

Nicholson KG, Abrams KR, Batham S, Medina MJ, Warren FC, Barer M, et al. Randomised controlled trial and health economic evaluation of the impact of diagnostic testing for influenza, respiratory syncytial virus and Streptococcus pneumoniae infection on the management of acute admissions in the elderly and high-risk 18- to 64-year-olds. Health technology assessment (Winchester, England). 2014;18(36):1-viii.

Onwuchekwa C, Moreo LM, Menon S, Machado B, Curcio D, Kalina W, et al. Under-ascertainment of Respiratory Syncytial Virus infection in adults due to diagnostic testing limitations: A systematic literature review and meta-analysis. The Journal of infectious diseases. 2023.

Pazmany P, Soos A, Hegyi P, Dohos D, Kiss S, Szakacs Z, et al. Inflammatory Biomarkers Are Inaccurate Indicators of Bacterial Infection on Admission in Patients With Acute Exacerbation of Chronic Obstructive Pulmonary Disease-A Systematic Review and Diagnostic Accuracy Network Meta-Analysis. Frontiers in medicine. 2021;8:639794.

Petrozzino JJ, Smith C, Atkinson MJ. Rapid diagnostic testing for seasonal influenza: an evidence-based review and comparison with unaided clinical diagnosis. The Journal of emergency medicine. 2010;39(4):476-90.e1.

Schierenberg A, Minnaard MC, Hopstaken RM, van de Pol AC, Broekhuizen BDL, de Wit NJ, et al. External Validation of Prediction Models for Pneumonia in Primary Care Patients with Lower Respiratory Tract Infection: An Individual Patient Data Meta-Analysis. PloS one. 2016;11(2):e0149895.

van der Meer V, Neven AK, van den Broek PJ, Assendelft WJJ. Diagnostic value of C reactive protein in infections of the lower respiratory tract: systematic review. BMJ (Clinical research ed). 2005;331(7507):26.

Vos LM, Bruning AHL, Reitsma JB, Schuurman R, Riezebos-Brilman A, Hoepelman AIM, et al. Rapid Molecular Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review of Diagnostic Accuracy and Clinical Impact Studies. Clinical

infectious diseases : an official publication of the Infectious Diseases Society of America. 2019;69(7):1243-53.

Wu M-H, Lin C-C, Huang S-L, Shih H-M, Wang C-C, Lee C-C, et al. Can procalcitonin tests aid in identifying bacterial infections associated with influenza pneumonia? A systematic review and meta-analysis. Influenza and other respiratory viruses. 2013;7(3):349-55.

1.1.14.2 Included primary studies for white cell different count

Castro-Guardiola A, Armengou-Arxe A, Viejo-Rodriguez AL, Penarroja-Matutano G, Garcia-Bragado F. Differential diagnosis between community-acquired pneumonia and non-pneumonia diseases of the chest in the emergency ward. European Journal of Internal Medicine. 2000;11(6):334-9.

Gulich MS, Matschiner A, Gluck R, Zeitler HP. Improving diagnostic accuracy of bacterial pharyngitis by near patient measurement of C-reactive protein (CRP). The British journal of general practice : the journal of the Royal College of General Practitioners. 1999;49(439):119-21.

Holm A, Nexoe J, Bistrup LA, Pedersen SS, Obel N, Nielsen LP, et al. Aetiology and prediction of pneumonia in lower respiratory tract infection in primary care. British Journal of General Practice. 2007;57(540):547-54.

Liu YF, Gao Y, Chen MF, Cao B, Yang XH, Wei L. Etiological analysis and predictive diagnostic model building of community-acquired pneumonia in adult outpatients in Beijing, China. BMC Infectious Diseases. 2013;13(1):309.

1.1.14.3 Included primary studies for multiplex PCR tests

Boku S, Naito T, Murai K, Tanei M, Inui A, Nisimura H, et al. Near point-of-care administration by the attending physician of the rapid influenza antigen detection immunochromatography test and the fully automated respiratory virus nucleic acid test: Contribution to patient management. Diagnostic Microbiology and Infectious Disease. 2013;76(4):445-9.

Escarate E, Jones CG, Clarke E, Clark P, Norton S, Bag S, et al. Rapid on-site molecular Point of Care Testing during influenza outbreaks in aged care facilities improves antiviral use and reduces hospitalisation. Australian and New Zealand journal of public health. 2022;46(6):884-8.

Farfour E, Yung T, Baudoin R, Vasse M. Evaluation of Four Fully Integrated Molecular Assays for the Detection of Respiratory Viruses during the Co-Circulation of SARS-CoV-2, Influenza and RSV. Journal of Clinical Medicine. 2022;11(14):3942.

Hansen GT, Moore J, Herding E, Gooch T, Hirigoyen D, Hanson K, et al. Clinical decision making in the emergency department setting using rapid PCR: Results of the CLADE study group. Journal of Clinical Virology. 2018;102:42-9.

Maignan M, Viglino D, Hablot M, Masson NT, Lebeugle A, Muret RC, et al. Diagnostic accuracy of a rapid RT-PCR assay for point-of-care detection of influenza A/B virus at

emergency department admission: A prospective evaluation during the 2017/2018 influenza season. PLoS ONE. 2019;14(5):e0216308.

Morris TC, Bird PW, Horvath-Papp E, Dhillon JK, May S, Tang JW. Xpert Xpress Flu/RSV: Validation and impact evaluation at a large UK hospital trust. Journal of Medical Virology. 2021;93(8):5146-51.

Peretz A, Zadok BS, Azrad M. Performance of the Influ a+B K-SeT assay as compared to two RT-PCR assays for detection of influenza virus. Diagnostic Microbiology and Infectious Disease. 2020;98(1):115097.

Tanei M, Yokokawa H, Murai K, Sakamoto R, Amari Y, Boku S, et al. Factors influencing the diagnostic accuracy of the rapid influenza antigen detection test (RIADT): A cross-sectional study. BMJ Open. 2014;4(1):e003885.

Valentin T, Kieslinger P, Stelzl E, Santner BI, Groselj-Strele A, Kessler HH, et al. Prospective evaluation of three rapid molecular tests for seasonal influenza in patients presenting at an emergency unit. Journal of Clinical Virology. 2019;111:29-32.

Yin N, Van Nuffelen M, Bartiaux M, Preseau T, Roggen I, Delaunoy S, et al. Clinical impact of the rapid molecular detection of RSV and influenza A and B viruses in the emergency department. PLoS ONE. 2022;17(9):e0274222.

Youngs J, Iqbal Y, Glass S, Riley P, Pope C, Planche T, et al. Implementation of the cobas Liat influenza point-of-care test into an emergency department during a high-incidence season: a retrospective evaluation following real-world implementation. Journal of Hospital Infection. 2019;101(3):285-8.

Zuurbier RP, Korsten K, Verheij TJM, Butler C, Adriaenssens N, Coenen S, et al. Performance Assessment of a Rapid Molecular Respiratory Syncytial Virus Point-of-Care Test: A Prospective Community Study in Older Adults. Journal of Infectious Diseases. 2022;226:S63-S70.

1.1.15 Contributors

Emily Brown (clinical advice)

Christie Cabral (primary care contextualization)

Deborah Caldwell (design, methodological advice, report editing, supervision)

Sarah Dawson (design, searching, report writing)

Alastair Hay (clinical advice)

Julian Higgins (design, methodological advice, report editing, supervision)

Hayley Jones (methodological advice, statistical analysis)

Tom Parkhouse (study selection, data extraction, analysis, GRADE, report writing)

Katie Webster (design, study selection, data extraction, analysis, GRADE, report writing)

Penny Whiting (design, methodological advice)

1.1.16 Acknowledgements

We would like to thank Elisa Gentilotti and Anna Gorska for providing additional data from their systematic review (Gentilotti et al. 2022) to assist in the preparation of this report.

Appendices

Appendix A – Review protocols

Review protocol for the diagnostic accuracy of near-patient, rapid tests to distinguish between bacterial and viral infection in suspected acute respiratory infection

	Diagnostic Accuracy
Participants	*Inclusion criteria:* • People aged 16 years or over with suspected acute respiratory infection, including (but not limited to) the following symptoms: o Cough or shortness of breath o Sore throat o Rhinitis *Exclusion criteria*: • Reviews that are exclusively in the following populations, or studies in which more than a quarter of the participants meet the following criteria: o People aged 16 years or over ▪ with known COVID-19. ▪ who are inpatients in hospital. ▪ who have a respiratory infection during end-of-life care. ▪ with aspiration pneumonia, bronchiectasis, cystic fibrosis (CF), or known immunosuppression. ▪ with symptoms of otitis media or sinusitis. o Children and young people under 16 years.
Index tests	*Inclusion criteria:* POCTs or symptoms and signs aiming to distinguish between viral and bacterial infection. We will include tests that: • Diagnose generic bacterial infection (i.e., any bacteria) • Diagnose generic viral infection (i.e., any virus) • Distinguish between a generic bacterial infection, a generic viral infection, and no infection We will also include tests that aim to identify the presence of the following specific pathogens: • Influenza (A+B)

<table>
<tr><td></td><td colspan="2">Diagnostic Accuracy</td></tr>
<tr><td></td><td colspan="2">• RSV

Exclusion criteria:
• POCTs for SARS-CoV-2 and group A streptococcus</td></tr>
<tr><td>Target</td><td colspan="2">Reference standard:
Any reference standard. We anticipate that this may include confirmation of bacterial infection or viral infection through laboratory testing, or defined via expert consensus, or a clinical algorithm.</td></tr>
<tr><td>Setting</td><td colspan="2">Inclusion criteria:
• Remote settings (via telephone, video call, online app, e-mail, or text message, e.g., NHS 111, 999 call centres or calls from GP practices)
• Face-to-face settings (e.g., the person’s home, a care home, primary care [including community pharmacy or acute respiratory infection hubs], NHS walk-in centres, emergency departments).

Exclusion criteria:
• Hospital inpatient settings</td></tr>
<tr><td>Studies</td><td>Systematic reviews of diagnostic accuracy studies. Systematic reviews will be identified by the use of all of the following:

○ clear and unambiguous eligibility criteria
○ comprehensive search (either stated as their aim or implied by use of 2 or more bibliographic databases)
○ details of included studies separately identifiable (for example with a table of characteristics, and references for all included studies)
○ the use of tools to assess the validity of primary studies (for example QUADAS-2).

We will seek to identify the most robust and up-to-date evidence for each test. Starting with the most recent published reviews, identified systematic reviews will be</td><td>If no good quality, applicable systematic reviews are identified, or where there are evidence gaps (for example missing index tests) in the systematic reviews, we will conduct searches for diagnostic test accuracy studies.
○ We will include one-gate designs (also known as diagnostic cross-sectional or diagnostic cohort studies).
○ Two gate designs (also known as diagnostic case-control studies) will be excluded.

Quantitative data on diagnostic test accuracy will be collected.</td></tr>
</table>

	Diagnostic Accuracy	
	assessed for their applicability, and those eligible will be quality assessed using published tools. Systematic reviews of good quality that closely match the review protocol will be extracted rather than extracting from the primary studies. Where multiple overlapping reviews are identified, we will include the most relevant review, considering the comprehensiveness of the search, date of publication and relevance to the current review question. Where a good quality review is found, earlier reviews with largely overlapping scope will not be assessed or extracted. Quantitative data on diagnostic test accuracy will be collected.	
Subgroup analyses	Where disaggregation is possible, we will repeat analyses according to the following subgroups: • setting of study (primary care, secondary care) • age of patient (65 years and under, 66 – 80 years, over 80 years) • presence of chronic co-morbidity (for example, COPD) • pregnancy and post-partum (up to 6 weeks) • different reference standards	
Other considerations	No date limitation will be applied. *Exclusions*: • studies not published in English • pre-prints • dissertations and theses • registry entries for ongoing clinical trials • editorials, letters, news items and commentaries • animal studies • conference abstracts and posters • derivation studies	

Appendix B – Literature search strategies

1. Systematic reviews of diagnostic test accuracy studies

Database: Ovid MEDLINE(R) ALL <1946 to May 22, 2023> Final search strategy

1	[Respiratory Tract Infection (RTI)]
2	exp Respiratory Tract Infections/
3	exp Otorhinolaryngologic Diseases/
4	((airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonar* tract or pulmonary or respirat* tract or respiratory or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (infect* or coinfect* or inflamm*)).tw,kf.
5	((chest or lung? or lobar or pleura?) adj3 (absces* or infect* or coinfect* or inflamm*)).tw,kf.
6	(bronchit* or bronchiolit* or allergic bronchopulmon* or bronchopneumon* or common cold* or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or laryngo tracheo bronchit* or laryngo tracheobronchit* or laryngotracheit* or nasopharyngit* or otitis media or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or severe acute respiratory syndrome or SARS or sinusit* or sore throat* or throat infection* or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or whooping cough or pertussis or pertusis).mp.
7	((acute* or exacerbat* or flare*) adj3 (asthma* or copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway* disease or chronic obstructive lung disease)).mp.
8	((acute* or subacute* or exacerbat* or prolonged) adj3 cough*).mp.
9	(RTI or LRTI or URTI or ARTI or AURI or ALRI).tw,kf.
10	or/2-9
11	[RTI Viral Infection]
12	exp Respiratory System/ and (exp Viruses/ or exp Virus Diseases/)
13	exp Pneumonia, Viral/ or *Orthomyxoviridae Infections/ or Influenza, Human/
14	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (nonbacter* or viral* or virus* or adenovir*)).tw,kf.
15	(rhinovir* or rhino* vir* or coryzavir* or coryza* vir* or influenzavir* or influenza* vir* or (H1N1 or H3N2) or parainfluenzavir* or parainfluenza* vir* or pneumovir* or pneumo* vir* or human metapneumovir* or human meta-pneumovir* or HMPV or respiratory syncytial vir*).mp. or RSV.tw,kf.
16	or/12-15
17	[RTI Bacterial Infection]
18	exp Respiratory System/ and (exp Bacteria/ or exp Bacterial Infections/)

19	Pneumonia, Bacterial/ or Chlamydial Pneumonia/ or Pneumonia, Mycoplasma/ or Pneumonia, Pneumococcal/ or Pneumonia, Staphylococcal/
20	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (bacter* or bacilli* or bacili* or corynebac* or mycobac* or nonvir* or pathogen*)).tw,kf.
21	(strep* pneumon* or diplococ* pneumon* or pneumococ* or staph* pneumon* or chlamyd* pneumon* or myco* pneumon* or influenza bacil* or bacteri* influenza* or h?emophil* influenza*).mp.
22	((strep* adj3 (throat* or pharyn* or tonsil*)) or (strep* and (airway* or pulmonary or brochopulmonar* or brocho-pulmonar* or respiratory* or (ear adj3 nose adj3 throat) or ENT or Otorhinolaryng*))).mp.
23	(GABHS or ("group a" adj3 strep*)).tw,kf.
24	strep* pyogen*.mp.
25	or/18-24
26	[Rapid Tests]
27	Point-of-Care Systems/
28	(POCT or POCTs or (((point adj2 care) or poc) adj3 (analys* or antigen? or assay* or device? or immunoassay* or classif* or detect* or determin* or diagnos* or differenti* or identif* or method* or kit or kits or panel? or platform? or predict* or rapid or routine* or screen* or system* or technique* or test* or (cassette? or dipstick? or film* or stick or strip or fluorescent anti*)))).tw,kf.
29	(point adj2 care).ti,kf.
30	(((near adj2 patient) or nearpatient or rapid* or bedside? or bed-side? or extra-laboratory or extralaboratory) adj3 (analys* or antigen? or assay* or immunoassay* or classif* or detect* or determin* or diagnos* or differenti* or identif* or method* or kit or kits or panel? or predict* or screen* or system* or technique* or test* or fluorescent anti*)).tw,kf.
31	(((near adj2 patient) or nearpatient or bedside? or bed-side? or extra-laboratory or extralaboratory) adj3 rapid*).tw,kf.
32	Rapid Diagnostic Tests/
33	(rapid* adj3 (detect* or diagnos* or screen*)).tw,kf.
34	(time-to-result? or ((quick* or rapid* or short* or time*) adj3 (turnaround or turn-around))).tw,kf.
35	(antigen? adj3 (analys* or assay* or immunoassay* or classif* or detect* or determin* or diagnos* or differenti* or identif* or method* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).tw,kf.
36	(RADT or RADTs or RDT or RDTs).tw,kf.
37	(biomarker* or bio* marker* or ((biologic* or bacteri* or viral or virus or immuno* or inflammat* or molecular or protein or serum) adj marker*)).tw,kf.
38	((rapid adj3 (molecular or PCR or polymerase chain reaction)) or singleplex* or single-plex* or multiplex* or multi-plex*).mp.
39	lab-on-a-chip.tw,kf.
40	((lateral flow adj (assay* or immunoassay* or test*)) or LFA or LFIA).tw,kf.
41	(immunochromatograph* or immuno-chromatograph* or immuno-chromato-graph* or direct immunofluorescence or direct immuno-fluorescence or enzym*

	immunoassay* or enzym* immuno-assay* or fluorescence immunoassay* or fluorescence immuno-assay* or optical immunoassay* or optical immuno-assay*).mp. or (ICA or EIA or FIA or OIA).tw,kf.
42	((chemiluminescen* or chemi-luminescen*) adj (immunoassay* or immuno-assay* or assay*)).mp.
43	(((mobile or portable or handheld or hand-held) adj3 (analy#er? or device? or meters or metres)) and (blood? or plasma or saliva or sputum or spit or mucus or urine or urea or urinalys* or fluids or gas or gases)).mp.
44	or/27-43
45	(10 or 16 or 25) and 44
46	[Systematic Review Filter]
47	(systematic review or meta-analysis).pt.
48	systematic review/ or meta-analysis/ or network meta-analysis/
49	(meta-analys* or metaanalys* or meta-synth* or metasynth*).tw,kf.
50	(((systematic* or quantitativ* or methodologic*) adj5 (review* or overview*)) or (systematic* adj3 analys*)).tw,kf.
51	(systematic or structured or evidence or diagnostic or predicti* or trials or studies).ti. and ((review or overview or look or examination or update* or summary).ti. or review.pt.)
52	(quantitativ$ adj5 synthes*).tw,kf.
53	((research adj3 (integrati* or overview*)) or (integrative adj2 review*) or research integration).tw,kf.
54	scoping review?.ti,kf. or (review.ti,kf,pt. and (trials as topic or studies as topic).hw.)
55	((diagnostic or evidence) adj3 review*).tw,kf.
56	review.pt. and (medline or medlars or embase or pubmed or scisearch or psychinfo or psycinfo or psychlit or psyclit or cinahl or electronic database* or bibliographic database* or computeri#ed database* or online database* or pooling or pooled or mantel haenszel or peto or dersimonian or der simonian or fixed effect or ((hand adj2 search*) or (manual* adj2 search*))).tw,kf,hw.
57	exp technology assessment, biomedical/
58	(technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).tw,kf.
59	(0266-4623 or 1469-493X or 1366-5278 or 1530-440X or 2046-4053).is.
60	or/47-59
61	[DTA Filter]
62	Diagnosis/
63	"Diagnostic Techniques and Procedures"/
64	Diagnostic Test Approval/
65	Diagnostic Tests, Routine/
66	Molecular Diagnostic Techniques/
67	exp Reagent Kits, Diagnostic/
68	(diagnos* adj3 (analys* or assay* or immunoassay* or classif* or differenti* or method* or kit or kits or panel? or predict* or screen* or system* or technique* or test*)).ab.
69	diagnos*.ti,kf,hw.

70	"sensitivity and specificity"/ or "predictive value of tests"/ or roc curve/ or signal-to-noise ratio/ or "limit of detection"/
71	false negative reactions/ or false positive reactions/
72	(sensitivity or specificity).tw,kf.
73	likelihood ratio.tw,kf.
74	(predict* adj4 val*).tw,kf. or predict*.ti.
75	((accura* or reliab* or valid*) and (point-of-care or POC or (rapid adj2 (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*)))).tw,kf.
76	((accura* or reliab* or valid*) and (bacteri* and (viral or virus*) and (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*))).tw,kf.
77	area under curve/
78	(observer adj variation*).tw,kf.
79	(roc adj curve*).tw,kf.
80	likelihood functions/
81	(false adj (positiv* or negativ*)).tw,kf.
82	QUADAS*.mp.
83	Diagnosis, Differential/
84	(codetect* or co-detect* or codiagnos* or co-diagnos*).tw,kf.
85	((discriminat* or differenti* or dual*) adj (detect* or diagnos*)).mp.
86	(bacteri* adj5 (viral or virus*) adj5 (analys* or assay* or immunoassay* or classif* or detect* or codetect* or determin* or diagnos* or codiagnos* or differenti* or discriminat* or distinguish* or identif* or method* or misdiagnos* or predict* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).tw,kf,hw.
87	or/62-86
88	45 and 60 and 87
89	[Other]
90	(bacteri* adj5 (viral or virus*) adj5 (detect* or diagnos* or differenti* or predict* or screen* or test*)).tw,kf.
91	(bacteri* and (viral or virus*) and (codetect* or co-detect* or codiagnos* or co-diagnos*)).tw,kf.
92	(10 or 16 or 25) and 60 and (90 or 91)
93	(((prescribing or prescription?) adj guideline?) or ((antibiotic? or antimicrobial) adj stewardship?)).mp.
94	((guide or guiding or predict* or ration* or reduc* or steward*) adj3 (antibiotic* or antivir* or anti-vir* or antimicrob* or anti-microb*)).tw,kf.
95	45 and 60 and (93 or 94)
96	88 or 92 or 95
97	remove duplicates from 96
98	[Symptoms & Signs]
99	Symptom Assessment/
100	Patient Acuity/
101	((sign? adj3 symptom*) or ((sign? or symptom*) adj2 (score* or scoring))).tw,kf.
102	((patient* or sign? or symptom* or illness* or disease* or disorder* or infection*) adj3 acuity).tw,kf.

103	exp Vital Signs/
104	(peak flow or oxygen saturation or sats).mp.
105	Clinical Decision Rules/
106	(clinic* predicti* or (clinic* adj5 (decision* or predicti*) adj5 (aid? or algorithm? or characteristic? or criteri* or evaluation? or index or indices or marker? or method* or model* or panel? or parameter? or rule or rules or score? or scoring or screen* or signs or symptoms or system? or technique? or test* or tool? or value? or variable*))).mp.
107	(clinical* adj (predicti* or predictor*)).tw,kf.
108	(rule in or ruled in or rule out or ruled out).tw,kf.
109	((predict* or prognos* or cluster*) adj3 (sign? or symptom*)).tw,kf.
110	((detect* or diagnos*) adj5 (sign? or symptom*)).tw,kf.
111	or/99-110
112	(10 or 16 or 25) and 111 and 60 and 87
113	[Host-response biomarkers]
114	Procalcitonin/
115	(procalcitonin or pro-calcitonin or calcitonin precursor polyprotein or calcitonin related polypeptide alpha or calcitonin-1).mp. or PCT.tw,kf.
116	C-Reactive Protein/
117	C-reactive protein.mp. or (CRP or HSCRP).tw,kf.
118	Myxovirus Resistance Proteins/
119	(myxovirus resistance protein* or mx-protein* or MxA or (interferon adj2 induc* protein) or IP-10).mp.
120	(myxovirus resistance protein* or mx-protein* or MxA or (interferon adj2 induc* protein)).mp.
121	(FebriDx* or Febri-Dx*).mp.
122	TNF-Related Apoptosis-Inducing Ligand/
123	((tumor necrosis factor or TNF) adj2 related apoptosis adj2 ligand).tw,kf.
124	TRAIL.tw,kf.
125	Chemokine CXCL10/
126	(ImmunoXpert* or Immuno-Xpert*).tw,kf.
127	(Interferon gamma inducible protein-10 or IFN-gamma-inducible protein-10 or IP-10 or IP10 or CXCL10 or CXCL-10).tw,kf.
128	(ImmunoXpert* or Immuno-Xpert* or MeMedBV* or MeMed-BV*).mp.
129	leukocyte count/ or lymphocyte count/ or cd4 lymphocyte count/ or cd4-cd8 ratio/
130	((WBC or white blood cell? or lymphocyte? or leukocyte? or CD4 or eosinophil? or neutrophil?) adj3 (count? or number? or ratio?)).tw,kf.
131	*leukocytes/ or exp *granulocytes/ or exp *leukocytes, mononuclear/
132	*interleukins/ or interleukin-5/ or interleukin-6/ or interleukin-10/
133	(il-5 or interleukin 5 or b-cell-growth-factor-ii or bcgf-ii or eosinophil differentiation factor or t-cell replacing factor).tw,kf.
134	(il-6 or interleukin-6 or b-cell differentiation factor or b-cell stimulatory factor-2 or bsf-2 or (differentiation-inducing protein adj1 myeloid) or hybridoma growth factor or plasmacytoma growth factor or hepatocyte stimulating factor or interferon beta-2 or ifn-beta-2 or mgi-2).tw,kf.
135	(il-10 or interleukin-10 or cytokine synthesis inhibitory factor or csif-10).tw,kf.

136	(interleukin*.tw,kf. or exp Interleukins/) and ((diagnos* or detect*).ti,kf,hw. or diagnosis.fs.)
137	or/114-136
138	(10 or 16 or 25) and 137 and 60 and 87
139	HEMATOLOGIC TESTS/
140	((h?em* or blood or plasma or serum) adj2 (test* or marker?)).tw,kf.
141	exp Cell Count/
142	((blood or RBC or red cell? or erythrocyt* or normocyt* or platelet* or thrombocyt*) adj3 (count* or distribution? or number* or paramet* or ratio?)).tw,kf.
143	Blood Sedimentation/
144	(((blood or RBC or red cell? or erythrocyt*) adj2 sedimentation) or ESR).tw,kf.
145	exp BLOOD GAS ANALYSIS/
146	blood gas*.tw,kf.
147	Oxygen/an, bl [Analysis, Blood]
148	Carbon Dioxide/an, bl [Analysis, Blood]
149	Sodium Bicarbonate/an, bl [Analysis, Blood]
150	(ABG or O2sat* or O2-sat* or O2CT or PaO2 or PaCO2 or HCO3 or (blood adj3 pH)).tw,kf.
151	(partial pressure and oxygen).hw.
152	(partial pressure adj3 (oxygen or O2)).tw,kf.
153	Sodium/bl [Blood]
154	((blood or plasma or serum) adj2 (sodium or Na)).tw,kf.
155	((blood or plasma or serum) adj2 marker?).tw,kf.
156	Fibrin Fibrinogen Degradation Products/
157	(fibrin* adj2 degradation).tw,kf.
158	fibrinogen.tw,kf. or *fibrinogen/ or Fibrinogen/an, bl, ur [Analysis, Blood, Urine]
159	(d-dimer? or ddimer?).tw,kf.
160	Urine/an [Analysis]
161	(((urin* or urea) adj2 (analys* or test* or marker?)) or UAT).tw,kf.
162	Nitrogen/ur [Urine]
163	((nitrogen or nitrate? or nitrite? or "N" or N2) adj3 (urea or urin*)).tw,kf.
164	Adrenomedullin/
165	(adrenomedullin or proadrenomedullin or ADM or proADM).tw,kf.
166	exp Aspartate Aminotransferases/
167	((aspartat* adj3 (aminotrans* or amino-trans* or apoaminotrans* or apo-aminotrans* or apo-amino-trans* or apoamino-trans* or transaminas* or trans-aminas*)) or ((glutam* aspart* or glutam* oxaloacet*) adj3 (transaminas* or trans-aminas*)) or sgot).tw,kf.
168	Alanine Transaminase/
169	((alanine adj3 (aminotrans* or amino-trans* or transamin* or trans-amin*)) or (glutam* adj3 pyruvic adj3 trans*) or sgpt).tw,kf.
170	((lipopolysac* or lipo-polysac* or lipo-poly-sac* or lipopoly-sac* or LPS) adj3 (bind* or bound*)).tw,kf.
171	Chitinases/ or Chitinase-3-like protein 1/

172	(kitinase-3-like-1 or chitinase-3-like-1 or chitinase-3-like-protein-1 or CHI3L1).tw,kf.
173	Antibodies, Bacterial/an, bl [Analysis, Blood]
174	Antibodies, Viral/an, bl [Analysis, Blood]
175	Blood Proteins/an
176	Immunoglobulins/an
177	("immunoglobulin M" or IgM or "immunoglobulin G" or IgG).tw,kf,hw.
178	*Serologic Tests/
179	(((point adj2 care) or poc or (near adj2 patient) or nearpatient or rapid* or bedside? or bed-side? or extra-laboratory or extralaboratory) adj3 (serolog* or antibody or antibodies or immunoglobulin* or immune globulin*)).tw,kf.
180	((serolog* or antibody or antibodies or immunoglobulin* or immune globulin*) and (analys* or assay* or immunoassay* or classif* or detect* or determin* or diagnos* or differenti* or identif* or method* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).ti,kf.
181	or/139-180
182	(10 or 16 or 25) and 181 and 60 and 87
183	97 or 112 or 138 or 182

Database: Ovid Embase <1974 to 2023 May 24>

1	Respiratory Tract Infection/ or exp Influenza/ or Laryngotracheobronchitis/ or Parainfluenza Virus Infection/ or Respiratory Syncytial Virus Infection/ or Viral Respiratory Tract Infection/ or Lower Respiratory Tract Infection/ or Chest Infection/ or Pertussis/ or Lung Infection/ or exp Infectious Pneumonia/ or Lung Abscess/ or exp Lung Mycosis/ or exp Viral Bronchiolitis/ or Upper Respiratory Tract Infection/ or exp Nose Infection/ or Oropharynx Candidiasis/ or Peritonsillar Abscess/ or Viral Upper Respiratory Tract Infection/
2	Ear Nose Throat Disease/di or Otorhinolaryngology/ or exp Ear Infection/ or exp Otitis/
3	((airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonar* tract or pulmonary or respirat* tract or respiratory or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (infect* or coinfect* or inflamm*)).tw,kf.
4	((chest or lung? or lobar or pleura?) adj3 (absces* or infect* or coinfect* or inflamm*)).tw,kf.
5	(bronchit* or bronchiolit* or allergic bronchopulmon* or bronchopneumon* or common cold* or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or laryngo tracheo bronchit* or laryngo tracheobronchit* or laryngotracheit* or nasopharyngit* or otitis media or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or severe acute respiratory syndrome or SARS or sinusit* or sore throat* or throat infection* or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or whooping cough or pertussis or pertusis).mp.

6	((acute* or exacerbat* or flare*) adj3 (asthma* or copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway* disease or chronic obstructive lung disease)).mp.
7	((acute* or subacute* or exacerbat* or prolonged) adj3 cough*).mp.
8	(RTI or LRTI or URTI or ARTI or AURI or ALRI).tw,kf.
9	or/1-8
10	exp Respiratory System/ and exp Virus Infection/
11	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (nonbacter* or viral* or virus* or adenovir*)).tw,kf.
12	Rhinovirus/ or exp Human Rhinovirus/ or exp Rhinovirus Infection/
13	exp Influenza Virus/ or Orthomyxovirus Infection/
14	Respirovirus/ or Human Parainfluenza virus 1/ or Human Parainfluenza Virus 3/ or Respirovirus Infection/
15	exp Virus Pneumonia/
16	Pneumovirus/ or Pneumovirus Infection/ or exp Human Respiratory Syncytial Virus/ or Respiratory Syncytial Virus Infection/
17	Metapneumovirus/ or Metapneumovirus Infection/ or Human Metapneumovirus/ or Human Metapneumovirus Infection/
18	(rhinovir* or rhino* vir* or coryzavir* or coryza* vir* or influenzavir* or influenza* vir* or (H1N1 or H3N2) or parainfluenzavir* or parainfluenza* vir* or pneumovir* or pneumo* vir* or human metapneumovir* or human meta-pneumovir* or HMPV or respiratory syncytial vir*).mp. or RSV.tw,kf.
19	or/10-18
20	exp Respiratory System/ and (exp Bacterium/ or exp Bacterial Infection/)
21	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (bacter* or bacilli* or bacili* or corynebac* or mycobac* or nonvir* or pathogen*)).tw,kf.
22	Bacterial Pneumonia/ or Chlamydial Pneumonia/ or Mycoplasma Pneumonia/ or Staphylococcal Pneumonia/ or exp Streptococcus Pneumonia/
23	(strep* pneumon* or diplococ* pneumon* or pneumococ* or staph* pneumon* or chlamyd* pneumon* or myco* pneumon* or influenza bacil* or bacteri* influenza* or h?emophil* influenza*).mp.
24	((strep* adj3 (throat* or pharyn* or tonsil*)) or (strep* and (airway* or pulmonary or brochopulmonar* or brocho-pulmonar* or respiratory* or (ear adj3 nose adj3 throat) or ENT or Otorhinolaryng*))).mp.
25	Streptococcus Infection/ or Streptococcus Group A/ or exp Group A Streptococcal Infection/ or Streptococcal Pharyngitis/
26	(GABHS or ("group a" adj3 strep*)).tw,kf.
27	strep* pyogen*.mp.
28	or/20-27
29	"systematic review"/ or meta analysis/ or network meta-analysis/
30	review.pt. and (evidence based adj (medicine or practice)).mp.

31	(systematic or structured or evidence or diagnostic or predicti* or trials or studies).ti. and ((review or overview or look or examination or update* or summary).ti. or review.pt.)
32	(0266-4623 or 1469-493X or 1366-5278 or 1530-440X or 2046-4053).is.
33	(systematic review? or evidence report* or technology assessment?).jw.
34	(meta-analys* or metaanalys* or meta-synth* or metasynth*).ti,ab,kf,hw.
35	(((systematic* or methodologic*) adj3 (analys* or review* or overview*)) or (quantitativ* adj3 (review* or synthes*))).tw,kf.
36	(diagnostic test accuracy study or validation study or cohort analysis or cross-sectional study or case control study).hw. and review.ti,kf,pt.
37	((integrative adj2 review*) or research integration).tw,kf. or scoping review?.ti,kf.
38	((diagnostic or evidence) adj3 review*).tw,kf.
39	review.pt. and (medline or medlars or embase or pubmed or scisearch or psychinfo or psycinfo or psychlit or psyclit or cinahl or electronic database* or bibliographic database* or computeri#ed database* or online database* or pooling or pooled or mantel haenszel or peto or dersimonian or der simonian or fixed effect or ((hand adj2 search*) or (manual* adj2 search*))).ti,ab,kf,hw.
40	biomedical technology assessment/
41	(technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).tw,kf.
42	or/29-41
43	Gold Standard/
44	(reference standard? or gold standard?).tw,kf.
45	clinical diagnosis.mp.
46	Diagnostic Test Accuracy Study/
47	Diagnostic Accuracy /
48	(DTA or (diagnos* adj2 accura*)).tw,kf.
49	Validation Study/
50	"Sensitivity and Specificity"/
51	specificity.tw,kf.
52	Receiver Operating Characteristic/
53	Reliability/
54	Internal Validity/
55	Internal Consistency/
56	(validat* or validity).tw,kf.
57	likelihood ratio*.tw,kf.
58	Predictive Value/
59	(predict* adj4 val*).tw,kf. or predict*.ti.
60	((re-test or retest or test-retest) adj reliability).tw,kf.
61	Diagnostic Error/ or False Negative Result/ or False Positive Result/ or Missed Diagnosis/
62	(false adj (positiv* or negativ*)).tw,kf.
63	receiver operating characteristic*.tw,kf.
64	ROC.tw,kf.
65	Area Under the Curve/
66	Observer Variation/

67	(observer adj variation*).tw,kf.
68	((degree? or rate* or rating) adj3 agreement?).tw,kf.
69	Diagnosis/
70	diagnos*.ti,kf.
71	(diagnos* adj3 (analys* or assay* or immunoassay* or classif* or differenti* or method* or kit or kits or panel? or predict* or screen* or system* or technique* or test*)).ab.
72	Diagnostic Procedure/ or Diagnostic Test/ or Diagnostic Test Approval/ or exp Diagnostic Kit/ or Diagnosis Time/
73	Laboratory Diagnosis/
74	Molecular Diagnosis/
75	((accura* or reliab* or valid*) and (point-of-care or POC or (rapid adj2 (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*))))).tw,kf.
76	((accura* or reliab* or valid*) and (bacteri* and (viral or virus*) and (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*))).tw,kf.
77	"quality assessment of diagnostic accuracy studies"/
78	QUADAS*.mp.
79	Differential Diagnosis/
80	(codetect* or co-detect* or codiagnos* or co-diagnos*).tw,kf.
81	((discriminat* or differenti* or dual*) adj (detect* or diagnos*)).mp.
82	(bacteri* adj5 (viral or virus*) adj5 (analys* or assay* or immunoassay* or classif* or detect* or codetect* or determin* or diagnos* or codiagnos* or differenti* or discriminat* or distinguish* or identif* or method* or misdiagnos* or predict* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).tw,kf,hw.
83	or/43-82
84	42 and 83
85	Diagnostic Accuracy/ and Review/
86	84 or 85
87	(9 or 19 or 28) and 86
88	(COVID19 or COVID-19 or COVID2019 or COVID-2019 or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2" or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2").ti.
89	87 not 88
90	((neonat* or infant* or child* or p?ediatri*) not adult*).ti.
91	89 not 90
92	"Point of Care System"/
93	(POCT or POCTs or (((point adj2 care) or poc) adj3 (analys* or antigen? or assay* or device? or immunoassay* or classif* or detect* or determin* or diagnos* or differenti* or identif* or method* or kit or kits or panel? or platform? or predict* or rapid or routine* or screen* or system* or technique* or test* or (cassette? or dipstick? or film* or stick or strip or fluorescent anti*))))).tw,kf.
94	(point adj2 care).ti,kf.

95	(((near adj2 patient) or nearpatient or rapid* or bedside? or bed-side? or extra-laboratory or extralaboratory) adj3 (analys* or antigen? or assay* or immunoassay* or classif* or detect* or determin* or diagnos* or differenti* or identif* or method* or kit or kits or panel? or predict* or screen* or system* or technique* or test* or fluorescent anti*)).tw,kf.
96	(((near adj2 patient) or nearpatient or bedside? or bed-side? or extra-laboratory or extralaboratory) adj3 rapid*).tw,kf.
97	Rapid Test/ or Influenza A Rapid Test/ or Streptococcus Group A Rapid Test/
98	(rapid test* or (rapid* adj3 (detect* or diagnos* or screen*))).tw,kf.
99	(time-to-result? or ((quick* or rapid* or short* or time*) adj3 (turnaround or turn-around))).tw,kf.
100	(antigen? adj3 (analys* or assay* or immunoassay* or classif* or detect* or determin* or diagnos* or differenti* or identif* or method* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).tw,kf.
101	(RADT or RADTs or RDT or RDTs).tw,kf.
102	(biomarker or bio* marker* or ((biologic* or bacteri* or viral or virus or immuno* or inflammat* or molecular or protein or serum) adj marker*)).tw,kf.
103	Multiplex Analyzer/
104	exp Multiplex Polymerase Chain Reaction/
105	Singleplex Polymerase Chain Reaction/
106	((rapid adj3 (molecular or PCR or polymerase chain reaction)) or singleplex* or single-plex* or multiplex* or multi-plex*).mp.
107	lab-on-a-chip.tw,kf.
108	((lateral flow adj (assay* or immunoassay* or test*)) or LFA or LFIA).tw,kf.
109	(immunochromatograph* or immuno-chromatograph* or immuno-chromato-graph* or direct immunofluorescence or direct immuno-fluorescence or enzym* immunoassay* or enzym* immuno-assay* or fluorescence immunoassay* or fluorescence immuno-assay* or optical immunoassay* or optical immuno-assay*).mp. or (ICA or EIA or FIA or OIA).tw,kf.
110	((chemiluminescen* or chemi-luminescen*) adj (immunoassay* or immuno-assay* or assay*)).mp.
111	(((mobile or portable or handheld or hand-held) adj3 (analy#er? or device? or meters or metres)) and (blood? or plasma or saliva or sputum or spit or mucus or urine or urea or urinalys* or fluids or gas or gases)).mp.
112	or/92-111
113	91 and 112
114	(bacteri* adj5 (viral or virus*) adj5 (detect* or diagnos* or differenti* or predict* or screen* or test*)).tw,kf.
115	(bacteri* and (viral or virus*) and (codetect* or co-detect* or codiagnos* or co-diagnos*)).tw,kf.
116	(9 or 19 or 28) and 42 and (114 or 115)
117	116 not (88 or 90)
118	113 or 117
119	limit 118 to conference abstract status
120	118 not 119
121	Health Status Indicator/ or Patient Acuity/

122	Symptom Assessment/
123	Symptomatology/
124	*Symptom/
125	((sign? adj2 symptom*) and (score* or scoring)).tw,kf.
126	((patient* or sign? or symptom* or illness* or disease* or disorder* or infection*) adj3 acuity).tw,kf.
127	Vital Sign/
128	Decision Support System/ or Clinical Decision Rule/
129	(clinic* predicti* or (clinic* adj5 (decision* or predicti*) adj5 (aid? or algorithm? or characteristic? or criteri* or evaluation? or index or indices or marker? or method* or model* or panel? or parameter? or rule or rules or score? or scoring or screen* or signs or symptoms or system? or technique? or test* or tool? or value? or variable*))).tw,kf.
130	(clinical* adj (predicti* or predictor*)).tw,kf.
131	("rule in" or "ruled in" or "rule out" or "ruled out").tw,kf.
132	((predict* or prognos* or cluster*) adj3 (sign? or symptom*)).tw,kf.
133	((detect* or diagnos*) and (sign? or symptom*)).ti,kf.
134	or/121-133
135	91 and 134
136	limit 135 to conference abstract status
137	135 not 136
138	Procalcitonin Test Kit/
139	*Procalcitonin/ or Procalcitonin/ec [Endogenous Compound]
140	(procalcitonin or pro-calcitonin or calcitonin precursor polyprotein or calcitonin related polypeptide alpha or calcitonin-1 or PCT).tw,kf.
141	*C reactive protein/ or C reactive protein/ec [Endogenous Compound]
142	(c-reactive protein or CRP or HSCRP).tw,kf.
143	Myxovirus Resistance Protein/
144	(myxovirus resistance protein* or mx-protein* or MxA or (interferon adj2 induc* protein) or IP-10).tw,kf.
145	(FebriDx* or Febri-Dx*).af.
146	Tumor Necrosis Factor Related Apoptosis Inducing Ligand/
147	((tumor necrosis factor or TNF) adj2 related apoptosis adj2 ligand).tw,kf.
148	TRAIL.tw,kf.
149	C Reactive Protein/ and Endogenous Compound/
150	Procalcitonin/ and Endogenous Compound/
151	Gamma Interferon Inducible Protein 10/
152	(Interferon gamma inducible protein-10 or IFN-gamma-inducible protein-10 or IP-10 or IP10 or CXCL10 or CXCL-10).tw,kf.
153	(ImmunoXpert* or Immuno-Xpert* or MeMedBV* or MeMed-BV*).af.
154	or/138-153
155	91 and 154
156	limit 155 to conference abstract status
157	155 not 156
158	exp *Blood Cell Count/

159	((WBC or white blood cell? or white cell? or lymphocyte? or leukocyte? or monocyte? or CD4* or eosinophil? or neutrophil?) adj3 (count* or distribution? or number* or paramet* or ratio?)).tw,kf.
160	((whole blood or blood cell or RBC or red cell? or erythrocyt* or normocyt* or platelet* or thrombocyt*) adj3 (count* or distribution? or number* or paramet* or ratio?)).tw,kf.
161	((h?em* or blood or plasma or serum) adj2 (test* or marker?)).tw,kf.
162	*erythrocyte sedimentation rate/
163	(((blood or RBC or red cell? or erythrocyt*) adj2 sedimentation) or ESR).tw,kf.
164	or/158-163
165	91 and 164
166	limit 165 to conference abstract status
167	165 not 166
168	Blood Gas Analysis/
169	blood gas*.tw,kf.
170	Oxygen Saturation/
171	(ABG or O2sat* or O2-sat* or O2CT or PaO2 or PaCO2 or HCO3 or (blood adj3 pH)).tw,kf.
172	((oxygen adj2 (concentration or saturation)) or sats).tw,kf.
173	(partial pressure and oxygen).hw.
174	(partial pressure adj3 (oxygen or O2)).tw,kf.
175	or/168-174
176	91 and 175
177	((blood or plasma or serum) adj2 (sodium or Na)).tw,kf.
178	electrolyte blood level/ or sodium blood level/
179	(177 or 178) and 91
180	(il-5 or interleukin 5 or b-cell-growth-factor-ii or bcgf-ii or eosinophil differentiation factor or t-cell replacing factor or il-6 or interleukin-6 or b-cell differentiation factor or b-cell stimulatory factor-2 or bsf-2 or (differentiation-inducing protein adj1 myeloid) or hybridoma growth factor or plasmacytoma growth factor or hepatocyte stimulating factor or interferon beta-2 or ifn-beta-2 or mgi-2 or il-10 or interleukin-10 or cytokine synthesis inhibitory factor or csif-10).tw,kf.
181	180 and 91
182	fibrinogen/
183	fibrinogen.tw,kf.
184	fibrin degradation product/
185	(fibrin* adj2 degradation).tw,kf.
186	d dimer/
187	(d-dimer? or ddimer?).tw,kf.
188	or/182-187
189	91 and 188
190	(((urin* or urea) adj2 (analys* or test* or marker?)) or UAT).tw,kf.
191	((nitrogen or nitrate? or nitrite? or "N" or N2) adj3 (urea or urin*)).tw,kf.
192	urea nitrogen blood level/
193	urea/ec
194	or/190-193

195	194 and 91
196	Adrenomedullin/
197	(adrenomedullin or adrenomedullin or proadrenomedullin or proadrenomedullin or ADM or proADM).tw,kf.
198	(196 or 197) and 91
199	Enzyme Blood Level/
200	Aspartate Aminotransferase Blood Level/ or Aspartate Aminotransferase Level/
201	((aspartat* adj3 (aminotrans* or amino-trans* or apoaminotrans* or apo-aminotrans* or apo-amino-trans* or apoamino-trans* or transaminas* or trans-aminas*)) or ((glutam* aspart* or glutam* oxaloacet*) adj3 (transaminas* or trans-aminas*)) or sgot).tw,kf.
202	*Aspartate Aminotransferase/ or Aspartate Aminotransferase/ec [Endogenous Compound]
203	Alanine Aminotransferase Level/ or Alanine Aminotransferase Blood Level/
204	*Alanine Aminotransferase/ or Alanine Aminotransferase/ec [Endogenous Compound]
205	((alanine adj3 (aminotrans* or amino-trans* or transamin* or trans-amin*)) or (glutam* adj3 pyruvic adj3 trans*) or sgpt).tw,kf.
206	or/199-205
207	91 and 206
208	Lipopolysaccharide Binding Protein/ec [Endogenous Compound]
209	((lipopolysac* or lipo-polysac* or lipo-poly-sac* or lipopoly-sac* or LPS) adj3 (bind* or bound*)).tw,kf.
210	(208 or 209) and 91
211	Chitinase 3 Like Protein 1/
212	(kitinase-3-like-1 or chitinase-3-like-1 or chitinase-3-like-protein-1 or CHI3L1).tw,kf.
213	(211 or 212) and 91
214	(176 or 179 or 181 or 189 or 195 or 198 or 207 or 210 or 213)
215	limit 214 to conference abstract status
216	214 not 215
217	120 or 137 or 157 or 167 or 216

Database: Cochrane Database of Systematic Reviews
https://www.cochranelibrary.com/cdsr/reviews
Issue 5 of 12, May 2023 (searched 18 May 2023)
Records screened in situ for potentially relevant reviews

S1	All-Text: * Limit CDSR to Review Type: <Diagnostic>
S2	All-Text: * Limit CDSR to Protocol Type: <Diagnostic>

Database: NIHR Journal Library
https://www.journalslibrary.nihr.ac.uk/advancedsearch/

Browsed online, using NHIR Library indexing categories to help identify relevant DTA reviews. A series of short iterative searches were also conducted. Records were screened in-situ (30 May 2023).

Browsing

S1	NIHR Programme: <Systematic Reviews> Limited by: (i) HRCS Health Category: <Respiratory> or (ii) HRCS Health Category: <Infection>
S2	NIHR Programme: <HTA> Limited by:(i) HRCS Health Category: <Respiratory> or (ii) HRCS Health Category: <Infection>
S3	Research Type: <Evidence Synthesis> Limited by: (i) HRCS Health Category: <Respiratory> or (ii) HRCS Health Category: <Infection>
S4	Research Type: NICE DAR (Diagnostic Assessment Report)

Searching

S1	diagnos* AND review
S2	diagnos* AND accuracy
S3	diagnos* AND test*
S4	rapid* AND test*
S5	“point of care”

Database: Epistemonikos
https://www.epistemonikos.org/en/advanced_search

S1a	(respiratory OR “ear nose and throat” OR ENT OR otorhinolaryng* OR RTI OR LRTI OR URTI OR ARTI OR AURI OR ALRI OR airway* OR bronchopulmonar* OR broncho-pulmonar* OR tracheobronch* OR tracheo-bronch* OR “pulmonary tract” OR ((chest OR lung OR lungs OR lobar OR pleura*) AND (absces* OR infect* OR coinfect* OR inflamm*)) OR bronchit* OR bronchiolit* OR bronchopneumon* OR “common cold” OR coryza OR croup OR empyem* OR epipharyngit* OR epiglottit* OR epiglotit* OR flu OR influenza OR laryngit* OR laryngotracheobronchit* OR (laryngo AND tracheo AND bronchit*) OR (laryngo AND tracheobronchit*) OR laryngotracheit* OR nasopharyngit* OR “otitis media” OR parainfluenza OR pharyngit* OR pleurisy OR pneumoni* OR pleuropneumoni* OR rhinit* OR rhinopharyngit* OR rhinosinusit* OR sinusit* OR “sore throat” OR (throat AND infection*) OR supraglottit* OR supraglotit* OR tonsillit* OR tonsilit* OR tracheit* OR “whooping cough” OR pertussis OR pertussis OR asthma* OR “COPD” OR “COAD” OR “chronic obstructive pulmonary disease” OR “chronic obstructive airway disease” OR “chronic obstructive airways disease” OR “chronic obstructive lung disease” OR ((acute or subacute* or exacerbat* or prolonged) AND cough*)) Limit-1: Publication Type: <Systematic Review> AND Type of Study:<Diagnostic Accuracy> OR Limit-2: Publication Type: <Systematic Review> AND Type of Study: <Prediction (Diagnostic)>

S1b	SARS OR "severe acute respiratory syndrome" Limit-1: Publication Type: <Systematic Review> AND Type of Study: <Diagnostic Accuracy> [All SARS-CoV2, records not downloaded] Limit-2: Publication Type: <Systematic Review> AND Type of Study: <Prediction (Diagnostic)>
S1c	(rhinovir* OR (rhino* AND vir*) OR coryzavir* OR (coryza* AND vir*) OR influenzavir* OR (influenza* AND vir*) OR (H1N1 OR H3N2) OR parainfluenzavir* OR (parainfluenza* AND vir*) OR pneumovir* OR (pneumo* AND vir*) OR metapneumovir* OR meta-pneumovir* OR HMPV OR RSV OR ("respiratory syncytial" AND vir*) OR (strep* AND pneumon*) OR (diplococ* AND pneumon*) OR pneumococ* OR (staph* AND pneumon*) OR (chlamyd* AND pneumon*) OR (myco* AND pneumon*) OR (influenza AND bacil*) OR (bacteri* AND influenza*) OR (hemophil* AND influenza*) OR (haemophil* AND influenza*) OR (strep* AND (throat* OR pharyn* OR tonsil* OR airway* OR pulmonary OR brochopulmonar* OR brocho-pulmonar* OR respiratory*)) OR GABHS or ("group a" AND strep*) OR (strep* AND pyogen*)) Limit-1: Publication Type: <Systematic Review> AND Type of Study: <Diagnostic Accuracy> OR Limit-2: Publication Type: <Systematic Review> AND Type of Study: <Prediction (Diagnostic)>
S2a	(("diagnostic accuracy" OR "diagnostic test accuracy" OR (diagnostic AND studies)) AND ((rapid* AND (detect* or method* or molecular or test*)) OR "near patient" OR "point of care" OR POCT* OR biomarker* OR panel OR panels) AND ("respiratory tract" or (respiratory AND infection*) OR "ear nose and throat" OR "ENT" OR otorhinolaryng* OR "RTI" OR "LRTI" OR "URTI" OR "ARTI" OR "AURI" OR "ALRI" OR airway* OR bronchopulmonar* OR broncho-pulmonar* OR tracheobronch* OR tracheo-bronch* OR "pulmonary tract" OR (pulmonary AND infection*) OR ((chest OR lung OR lungs OR lobar OR pleura*) AND (absces* OR infect* OR coinfect* OR inflamm*)) OR bronchit* OR bronchiolit* OR bronchopneumon* OR "common cold" OR coryza OR croup OR empyem* OR epipharyngit* OR epiglottit* OR epiglotit* OR flu OR influenza OR laryngit* OR laryngotracheobronchit* OR (laryngo AND tracheo AND bronchit*) OR (laryngo AND tracheobronchit*) OR laryngotracheit* OR nasopharyngit* OR "otitis media" OR parainfluenza OR pharyngit* OR pleurisy OR pneumoni* OR pleuropneumoni* OR rhinit* OR rhinopharyngit* OR rhinosinusit* OR sinusit* OR "sore throat" OR (throat AND infection*) OR supraglottit* OR supraglotit* OR tonsillit* OR tonsilit* OR tracheit* OR "whooping cough" OR pertussis OR pertussis OR asthma* OR "COPD" OR "COAD" OR "chronic obstructive pulmonary disease" OR "chronic obstructive airway disease" OR "chronic obstructive airways disease" OR "chronic obstructive lung disease" OR ((acute or subacute* or exacerbat* or prolonged) AND cough*))) Limit: Publication Type: <Systematic Review>
S2b	((diagnos* OR detect*) AND ("clinical decision rule" OR "clinical decision rules" OR "prediction model" OR "prediction models" OR "predictive model" OR "predictive models" OR "prediction rule" OR "prediction rules" OR "predictive rule" OR "predictive rules") AND ("respiratory tract" or (respiratory AND infection*) OR "ear nose and throat" OR "ENT" OR otorhinolaryng* OR "RTI" OR "LRTI" OR "URTI" OR "ARTI" OR "AURI" OR "ALRI" OR airway* OR

	bronchopulmonar* OR broncho-pulmonar* OR tracheobronch* OR tracheo-bronch* OR “pulmonary tract” OR (pulmonary AND infection*) OR ((chest OR lung OR lungs OR lobar OR pleura*) AND (absces* OR infect* OR coinfect* OR inflamm*)) OR bronchit* OR bronchiolit* OR bronchopneumon* OR “common cold” OR coryza OR croup OR empyem* OR epipharyngit* OR epiglottit* OR epiglotit* OR flu OR influenza OR laryngit* OR laryngotracheobronchit* OR (laryngo AND tracheo AND bronchit*) OR (laryngo AND tracheobronchit*) OR laryngotracheit* OR nasopharyngit* OR “otitis media” OR parainfluenza OR pharyngit* OR pleurisy OR pneumoni* OR pleuropneumoni* OR rhinit* OR rhinopharyngit* OR rhinosinusit* OR sinusit* OR “sore throat” OR (throat AND infection*) OR supraglottit* OR supraglotit* OR tonsillit* OR tonsilit* OR tracheit* OR “whooping cough” OR pertussis OR pertussis OR asthma* OR “COPD” OR “COAD” OR “chronic obstructive pulmonary disease” OR “chronic obstructive airway disease” OR “chronic obstructive airways disease” OR “chronic obstructive lung disease” OR ((acute or subacute* or exacerbat* or prolonged) AND cough*))) Limit: Publication Type: <Systematic Review>
S2c	((“diagnostic accuracy” OR “diagnostic test accuracy” OR (diagnostic AND studies)) AND ((rapid* AND (detect* or method* or molecular or test*)) OR “near patient” OR “point of care” OR POCT* OR biomarker* OR panel OR panels) AND (rhinovir* OR (rhino* AND vir*) OR coryzavir* OR (coryza* AND vir*) OR influenzavir* OR (influenza* AND vir*) OR (H1N1 OR H3N2) OR parainfluenzavir* OR (parainfluenza* AND vir*) OR pneumovir* OR (pneumo* AND vir*) OR metapneumovir* OR meta-pneumovir* OR HMPV OR RSV OR (“respiratory syncytial” AND vir*) OR (strep* AND pneumon*) OR (diplococ* AND pneumon*) OR pneumococ* OR (staph* AND pneumon*) OR (chlamyd* AND pneumon*) OR (myco* AND pneumon*) OR (influenza AND bacil*) OR (bacteri* AND influenza*) OR (hemophil* AND influenza*) OR (haemophil* AND influenza*) OR (strep* AND (throat* OR pharyn* OR tonsil* OR airway* OR pulmonary OR brochopulmonar* OR brocho-pulmonar* OR respiratory*)) OR GABHS or ("group a" AND strep*) OR (strep* AND pyogen*))) Limit: Publication Type: <Systematic Review>
S2d	((diagnos* OR detect*) AND (“clinical decision rule” OR “clinical decision rules” OR “prediction model” OR “prediction models” OR “predictive model” OR “predictive models” OR “prediction rule” OR “prediction rules” OR “predictive rule” OR “predictive rules”) AND (rhinovir* OR (rhino* AND vir*) OR coryzavir* OR (coryza* AND vir*) OR influenzavir* OR (influenza* AND vir*) OR (H1N1 OR H3N2) OR parainfluenzavir* OR (parainfluenza* AND vir*) OR pneumovir* OR (pneumo* AND vir*) OR metapneumovir* OR meta-pneumovir* OR HMPV OR RSV OR (“respiratory syncytial” AND vir*) OR (strep* AND pneumon*) OR (diplococ* AND pneumon*) OR pneumococ* OR (staph* AND pneumon*) OR (chlamyd* AND pneumon*) OR (myco* AND pneumon*) OR (influenza AND bacil*) OR (bacteri* AND influenza*) OR (hemophil* AND influenza*) OR (haemophil* AND influenza*) OR (strep* AND (throat* OR pharyn* OR tonsil* OR airway* OR pulmonary OR brochopulmonar* OR brocho-pulmonar* OR respiratory*)) OR GABHS or ("group a" AND strep*) OR (strep* AND pyogen*))) Limit: Publication Type: <Systematic Review>

2. Diagnostic test accuracy studies

White cell differential count

A precision maximising search was conducted due to the limited timeframe and inherent noise retrieved when searching for white blood cells and inflammatory infections

Database: Ovid MEDLINE(R) ALL <1946 to June 6, 2023>

1	Diagnosis/
2	"Diagnostic Techniques and Procedures"/
3	Diagnostic Test Approval/
4	Diagnostic Tests, Routine/
5	Molecular Diagnostic Techniques/
6	exp Reagent Kits, Diagnostic/
7	(diagnos* adj3 (analys* or assay* or immunoassay* or classif* or differenti* or method* or kit or kits or panel? or predict* or screen* or system* or technique* or test*)).ab.
8	diagnos*.ti,kf,hw.
9	(DTA or (diagnos* adj2 accura*)).tw,kf.
10	"sensitivity and specificity"/ or "predictive value of tests"/ or roc curve/ or signal-to-noise ratio/ or "limit of detection"/
11	(sensitivity or specificity).tw,kf.
12	likelihood ratio*.tw,kf.
13	(predict* adj4 val*).tw,kf. or predict*.ti.
14	((re-test or retest or test-retest) adj reliability).tw,kf.
15	((accura* or reliab* or valid*) and (point-of-care or POC or (rapid adj2 (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*)))).tw,kf.
16	((accura* or reliab* or valid*) and (bacteri* and (viral or virus*) and (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*))).tw,kf.
17	Validation Study/
18	(validat* or validity).tw,kf.
19	area under curve/
20	observer variation/
21	(observer adj variation*).tw,kf.
22	((degree? or rate* or rating) adj3 agreement?).tw,kf.
23	((detect* or diagnos*) and agreement?).tw,kf.
24	Receiver Operating Characteristic/
25	(receiver operating characteristic* or ROC).tw,kf.
26	likelihood functions/
27	diagnostic error/ or false negative result/ or false positive result/ or missed diagnosis/ or false negative reactions/ or false positive reactions/
28	(false adj (positiv* or negativ*)).tw,kf.
29	(QUADAS* or STARD).mp.

30	laboratory diagnosis/
31	(reference standard? or gold standard?).tw,kf.
32	Diagnosis, Differential/
33	(codetect* or co-detect* or codiagnos* or co-diagnos*).tw,kf.
34	((discriminat* or differenti* or dual*) adj (detect* or diagnos*)).mp.
35	(bacteri* adj5 (viral or virus*) adj5 (analys* or assay* or immunoassay* or classif* or detect* or codetect* or determin* or diagnos* or codiagnos* or differenti* or discriminat* or distinguish* or identif* or method* or misdiagnos* or predict* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).tw,kf,hw.
36	or/1-35
37	(((WBC or white blood cell? or white cell? or lymphocyte? or leukocyte? or monocyte? or CD4* or eosinophil? or neutrophil? or granulocyte?) adj3 (count* or distribution? or level? or number* or paramet* or ratio?)) or NLR).tw,kf.
38	(respiratory or (ear nose adj2 throat) or ENT or otorhinolaryng* or RTI or LRTI or URTI or ARTI or AURI or ALRI or airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonary tract or ((chest or lung or lungs or lobar or pleura*) and (absces* or infect* or coinfect* or inflamm*)) or bronchit* or bronchiolit* or bronchopneumon* or common cold or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or (laryngo and tracheo and bronchit*) or (laryngo and tracheobronchit*) or laryngotracheit* or nasopharyngit* or otitis media or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or sinusit* or sore throat or (throat and infection*) or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or whooping cough or pertussis or pertussis or asthma* or COPD or COAD or chronic obstructive pulmonary disease or chronic obstructive airway disease or chronic obstructive airways disease or chronic obstructive lung disease or ((acute or subacute* or exacerbat* or prolonged) and cough*)).ti.
39	36 and 37 and 38
40	(differential diagnos* or codetect* or co-detect*).mp.
41	((bacter* or bacilli* or bacili* or corynebac* or mycobac* or nonvir*) and (nonbacter* or viral* or virus* or adenovir*)).mp.
42	40 or 41
43	39 and 42
44	(((WBC or white blood cell? or white cell? or lymphocyte? or leukocyte? or monocyte? or CD4* or eosinophil? or neutrophil? or granulocyte?) and (count* or distribution? or level? or number* or paramet* or ratio?)) or NLR).ti.
45	38 and 42 and 44
46	43 or 45
47	(COVID19 or COVID-19 or COVID2019 or COVID-2019 or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2" or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2").ti.
48	46 not 47
49	((neonat* or infant* or child* or p?ediatri*) not adult*).ti.

50	48 not 49

Database: Ovid Embase <1980 to 2023 Week 22>

1	Gold Standard/
2	(reference standard? or gold standard?).tw,kf.
3	clinical diagnosis.mp.
4	Diagnostic Test Accuracy Study /
5	Diagnostic Accuracy /
6	(DTA or (diagnos* adj2 accura*)).tw,kf.
7	Validation Study/
8	"Sensitivity and Specificity"/
9	specificity.tw,kf.
10	Receiver Operating Characteristic/
11	Reliability/
12	Internal Validity/
13	Internal Consistency/
14	(validat* or validity).tw,kf.
15	likelihood ratio*.tw,kf.
16	predictive value/
17	(predict* adj4 val*).tw,kf. or predict*.ti.
18	((re-test or retest or test-retest) adj reliability).tw,kf.
19	diagnostic error/ or false negative result/ or false positive result/ or missed diagnosis/
20	(false adj (positiv* or negativ*)).tw,kf.
21	receiver operating characteristic*.tw,kf.
22	ROC.tw,kf.
23	area under the curve/
24	observer variation/
25	(observer adj variation*).tw,kf.
26	((degree? or rate* or rating) adj3 agreement?).tw,kf.
27	Diagnosis/
28	diagnos*.ti,kf.
29	(diagnos* adj3 (analys* or assay* or immunoassay* or classif* or differenti* or method* or kit or kits or panel? or predict* or screen* or system* or technique* or test*)).ab.
30	diagnostic procedure/ or diagnostic test/ or diagnostic test approval/ or exp diagnostic kit/ or diagnosis time/
31	laboratory diagnosis/
32	molecular diagnosis/
33	((accura* or reliab* or valid*) and (point-of-care or POC or (rapid adj2 (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*)))).tw,kf.
34	((accura* or reliab* or valid*) and (bacteri* and (viral or virus*) and (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*))).tw,kf.

35	"quality assessment of diagnostic accuracy studies"/
36	QUADAS*.mp.
37	differential diagnosis/
38	(codetect* or co-detect* or codiagnos* or co-diagnos*).tw,kf.
39	((discriminat* or differenti* or dual*) adj (detect* or diagnos*)).mp.
40	(bacteri* adj5 (viral or virus*) adj5 (analys* or assay* or immunoassay* or classif* or detect* or codetect* or determin* or diagnos* or codiagnos* or differenti* or discriminat* or distinguish* or identif* or method* or misdiagnos* or predict* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).tw,kf,hw.
41	or/1-40
42	(((WBC or white blood cell? or white cell? or lymphocyte? or leukocyte? or monocyte? or CD4* or eosinophil? or neutrophil? or granulocyte?) adj3 (count* or distribution? or level? or number* or paramet* or ratio?)) or NLR).tw,kf.
43	(respiratory or (ear nose adj2 throat) or ENT or otorhinolaryng* or RTI or LRTI or URTI or ARTI or AURI or ALRI or airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonary tract or ((chest or lung or lungs or lobar or pleura*) and (absces* or infect* or coinfect* or inflamm*)) or bronchit* or bronchiolit* or bronchopneumon* or common cold or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or (laryngo and tracheo and bronchit*) or (laryngo and tracheobronchit*) or laryngotracheit* or nasopharyngit* or otitis media or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or sinusit* or sore throat or (throat and infection*) or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or whooping cough or pertussis or pertussis or asthma* or COPD or COAD or chronic obstructive pulmonary disease or chronic obstructive airway disease or chronic obstructive airways disease or chronic obstructive lung disease or ((acute or subacute* or exacerbat* or prolonged) and cough*)).ti.
44	41 and 42 and 43
45	(differential diagnos* or codetect* or co-detect*).mp.
46	((bacter* or bacilli* or bacili* or corynebac* or mycobac* or nonvir*) and (nonbacter* or viral* or virus* or adenovir*)).mp.
47	45 or 46
48	44 and 47
49	(((WBC or white blood cell? or white cell? or lymphocyte? or leukocyte? or monocyte? or CD4* or eosinophil? or neutrophil? or granulocyte?) and (count* or distribution? or level? or number* or paramet* or ratio?)) or NLR).ti.
50	43 and 47 and 49
51	48 or 50
52	(COVID19 or COVID-19 or COVID2019 or COVID-2019 or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2" or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2").ti.
53	51 not 52
54	limit 53 to conference abstract status
55	53 not 54

56	((neonat* or infant* or child* or p?ediatri*) not adult*).ti.
57	55 not 56

Multiplex PCR

Database: Ovid MEDLINE(R) ALL <1946 to June 27, 2023> Final search strategy

1	[Target Conditions: RTI]
2	exp Respiratory Tract Infections/
3	exp Otorhinolaryngologic Diseases/
4	((airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonar* tract or pulmonary or respirat* tract or respiratory or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (infect* or coinfect* or inflamm*)).tw,kf.
5	((chest or lung? or lobar or pleura?) adj3 (absces* or infect* or coinfect* or inflamm*)).tw,kf.
6	(bronchit* or bronchiolit* or allergic bronchopulmon* or bronchopneumon* or common cold* or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or laryngo tracheo bronchit* or laryngo tracheobronchit* or laryngotracheit* or nasopharyngit* or otitis media or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or severe acute respiratory syndrome or SARS or sinusit* or sore throat* or throat infection* or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or whooping cough or pertussis or pertusis).mp.
7	((acute* or exacerbat* or flare*) adj3 (asthma* or copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway* disease or chronic obstructive lung disease)).mp.
8	((acute* or subacute* or exacerbat* or prolonged) adj3 cough*).mp.
9	(RTI or LRTI or URTI or ARTI or AURI or ALRI).tw,kf.
10	or/2-9
11	exp Respiratory System/ and (exp Viruses/ or exp Virus Diseases/)
12	exp pneumonia, viral/ or *orthomyxoviridae infections/ or influenza, human/
13	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (nonbacter* or viral* or virus* or adenovir*)).tw,kf.
14	(rhinovir* or rhino* vir* or coryzavir* or coryza* vir* or influenzavir* or influenza* vir* or (H1N1 or H3N2) or parainfluenzavir* or parainfluenza* vir* or pneumovir* or pneumo* vir* or human metapneumovir* or human meta-pneumovir* or HMPV or respiratory syncytial vir*).mp. or RSV.tw,kf.
15	or/11-14
16	exp Respiratory System/ and (exp Bacteria/ or exp Bacterial Infections/)
17	pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/
18	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (bacter* or bacilli* or bacili* or corynebac* or mycobac* or nonvir* or pathogen*)).tw,kf.

19	(strep* pneumon* or diplococ* pneumon* or pneumococ* or staph* pneumon* or chlamyd* pneumon* or myco* pneumon* or influenza bacil* or bacteri* influenza* or h?emophil* influenza*).mp.
20	((strep* adj3 (throat* or pharyn* or tonsil*)) or (strep* and (airway* or pulmonary or brochopulmonar* or brocho-pulmonar* or respiratory* or (ear adj3 nose adj3 throat) or ENT or Otorhinolaryng*))).mp.
21	(GABHS or ("group a" adj3 strep*)).tw,kf.
22	strep* pyogen*.mp.
23	or/16-22
24	10 or 15 or 23
25	[Index Tests: Rapid Multiplex Tests]
26	(multiplex* and "sample to answer").mp.
27	24 and 26
28	(maripoc* or mari-poc*).af.
29	(Rapid* and Diagnostic* and (MiniLab* or mini-lab*)).af.
30	(QIAstat* or QIA-stat* or (Qiagen* and (Resp* adj3 panel))).af.
31	(Biofire* Respiratory or Biofire* RP*).af.
32	(BioFire* adj (FilmArray* or Film-Array) adj (Respiratory Panel? or RP*)).af.
33	(Biofire* adj (FilmArray* or Film-Array*) adj Pneumo*).af.
34	(Biofire* adj (FilmArray* or Film-Array*)).ti.
35	(Biofire* and "sample to answer").mp.
36	(Biofire* adj5 (rapid or real time or RT-PCR or rRT-PCR)).mp.
37	(34 or 35 or 36) and 24
38	(Spotfire* or Spot-fire*).af.
39	24 and 38
40	(Cobas* adj5 ((lab* adj3 tube*) or liat*)).af.
41	24 and 40
42	(cobas* Influenza A* or cobas* Influenza B* or cobas* RSV or cobas* respiratory sync* virus).af.
43	((Cepheid* adj3 GeneXpert* adj3 Xpress*) or (Cepheid* adj3 Gene-Xpert* adj3 Xpress*)).af.
44	(Xpert* adj3 Xpress* adj3 (influenza or flu or respiratory sync* virus or RSV)).af.
45	(Cepheid* adj3 Xpert* adj3 (influenza or flu or respiratory sync* virus or RSV)).af.
46	(ePlex* RP* or (ePlex* adj3 resp* adj3 panel?)).af.
47	ePlex*.af.
48	24 and 47
49	((GenMark* or Gen-Mark*) and (RP* or (resp* adj3 panel?))).af.
50	(Simplexa* or Liaison* MDX*).af.
51	24 and 50
52	Aries*.mp. not (sheep or lamb or lambs or ram or rams or ewe or ewes or ovine or ovis aries).ti.
53	24 and 52
54	(Savanna* and (quidel* or molecular or multiplex* or rapid or real-time or RTPCR or RT-PCR or rRTPCR or rRT-PCR or test? or device? or panel? or PoCT or Point-of-Care or near-patient?)).mp.
55	24 and 54

56	((RVP4* or RVP-4*) and (Savanna* or Quidel* or molecular or multiplex* or rapid or real-time or RTPCR or RT-PCR or rRTPCR or rRT-PCR or test? or device? or panel? or PoCT or Point-of-Care or near-patient?)).mp.
57	(Respiratory Vir* Panel4* or Respiratory Vir* Panel-4*).af.
58	Verigen*.af.
59	24 and 58
60	Panther* Fusion*.af.
61	24 and 60
62	"Flu A/B/RSV*".af.
63	"AdV/hMPV/RV*".af.
64	"SARS-CoV-2/Flu A/B*".af.
65	"SARS-CoV-2/Flu A/B/RSV*".af.
66	(paraflu or parafluTM or parafluR).af.
67	27 or 28 or 29 or 30 or 31 or 32 or 33 or 37 or 39 or 41 or 42 or 43 or 44 or 45 or 46 or 48 or 49 or 51 or 53 or 55 or 56 or 57 or 59 or 61 or 62 or 63 or 64 or 65 or 66
68	((COVID19 or COVID-19 or COVID2019 or COVID-2019 or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2" or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2") not (rhinovir* or rhino* vir* or coryzavir* or coryza* vir* or influenzavir* or influenza* vir* or (H1N1 or H3N2) or parainfluenzavir* or parainfluenza* vir* or pneumovir* or pneumo* vir* or human metapneumovir* or human meta-pneumovir* or HMPV or respiratory sync* vir* or RSV)).ti.
69	67 not 68
70	(("SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2" or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2") adj3 Flu* adj3 RSV).af.
71	69 or 70
72	((neonat* or infant* or child* or p?ediatri*) not adult*).ti.
73	71 not 72

Database: Embase <1974 to 2023 June 27> Final search strategy

1	[Target Conditions:RTI]
2	respiratory tract infection/ or exp influenza/ or laryngotracheobronchitis/ or parainfluenza virus infection/ or respiratory syncytial virus infection/ or viral respiratory tract infection/ or lower respiratory tract infection/ or chest infection/ or pertussis/ or lung infection/ or exp infectious pneumonia/ or lung abscess/ or exp lung mycosis/ or exp viral bronchiolitis/ or upper respiratory tract infection/ or exp nose infection/ or oropharynx candidiasis/ or peritonsillar abscess/ or viral upper respiratory tract infection/
3	ear nose throat disease/di or otorhinolaryngology/ or exp ear infection/ or exp otitis/
4	((airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonar* tract or pulmonary or respirat* tract or respiratory

	or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (infect* or coinfect* or inflamm*)).tw,kf.
5	((chest or lung? or lobar or pleura?) adj3 (absces* or infect* or coinfect* or inflamm*)).tw,kf.
6	(bronchit* or bronchiolit* or allergic bronchopulmon* or bronchopneumon* or common cold* or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or laryngo tracheo bronchit* or laryngo tracheobronchit* or laryngotracheit* or legionnair* disease or legionellos* or middle east respiratory syndrome or MERS or nasopharyngit* or otitis media or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or severe acute respiratory syndrome or SARS or sinusit* or sore throat* or throat infection* or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or whooping cough or pertussis or pertusis).mp.
7	((acute* or exacerbat* or flare*) adj3 (asthma* or copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway* disease or chronic obstructive lung disease)).mp.
8	((acute* or subacute* or exacerbat* or prolonged) adj3 cough*).mp.
9	(RTI or LRTI or URTI or ARTI or AURI or ALRI).tw,kf.
10	or/2-9
11	exp respiratory system/ and exp virus infection/
12	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (nonbacter* or viral* or virus* or adenovir*)).tw,kf.
13	rhinovirus/ or exp human rhinovirus/ or exp rhinovirus infection/
14	exp Influenza virus/ or orthomyxovirus infection/
15	respirovirus/ or human parainfluenza virus 1/ or human parainfluenza virus 3/ or respirovirus infection/
16	exp virus pneumonia/
17	pneumovirus/ or pneumovirus infection/ or exp human respiratory syncytial virus/ or respiratory syncytial virus infection/
18	metapneumovirus/ or metapneumovirus infection/ or human metapneumovirus/ or human metapneumovirus infection/
19	(rhinovir* or rhino* vir* or coryzavir* or coryza* vir* or influenzavir* or influenza* vir* or (H1N1 or H3N2) or parainfluenzavir* or parainfluenza* vir* or pneumovir* or pneumo* vir* or human metapneumovir* or human meta-pneumovir* or HMPV or respiratory sync* vir*).mp. or RSV.tw,kf.
20	or/11-19
21	exp respiratory system/ and (exp bacterium/ or exp bacterial Infection/)
22	((airway* or respiratory or pulmonary or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or (ear adj3 nose adj3 throat) or ENT or otorhinolaryng*) adj3 (bacter* or bacilli* or bacili* or corynebac* or mycobac* or nonvir* or pathogen*)).tw,kf.
23	bacterial pneumonia/ or chlamydial pneumonia/ or mycoplasma pneumonia/ or staphylococcal pneumonia/ or exp streptococcus pneumonia/

24	(strep* pneumon* or diplococ* pneumon* or pneumococ* or staph* pneumon* or chlamyd* pneumon* or myco* pneumon* or influenza bacil* or bacteri* influenza* or h?emophil* influenza*).mp.
25	((strep* adj3 (throat* or pharyn* or tonsil*)) or (strep* and (airway* or pulmonary or brochopulmonar* or brocho-pulmonar* or respiratory* or (ear adj3 nose adj3 throat) or ENT or Otorhinolaryng*))).mp.
26	streptococcus infection/ or streptococcus group a/ or exp group a streptococcal infection/ or streptococcal pharyngitis/
27	(GABHS or ("group a" adj3 strep*)).tw,kf.
28	strep* pyogen*.mp.
29	or/21-28
30	10 or 20 or 29
31	[DTA Filter]
32	Gold Standard/
33	(reference standard? or gold standard?).tw,kf.
34	Diagnostic Test Accuracy Study/
35	Diagnostic Accuracy /
36	(DTA or (diagnos* adj2 accura*)).tw,kf.
37	Validation Study /
38	"Sensitivity and Specificity"/
39	(sensitivity or specificity).tw,kf.
40	Receiver Operating Characteristic/
41	Reliability/
42	Internal Validity/
43	Internal Consistency/
44	(validat* or validity).tw,kf.
45	likelihood ratio*.tw,kf.
46	predictive value/
47	(predict* adj4 val*).tw,kf. or predict*.ti.
48	((re-test or retest or test-retest) adj reliability).tw,kf.
49	diagnostic error/ or false negative result/ or false positive result/ or missed diagnosis/
50	(false adj (positiv* or negativ*)).tw,kf.
51	receiver operating characteristic*.tw,kf.
52	ROC.tw,kf.
53	area under the curve/
54	observer variation/
55	(observer adj variation*).tw,kf.
56	((degree? or rate* or rating) adj3 agreement?).tw,kf.
57	((detect* or diagnos*) and agreement?).tw,kf.
58	diagnostic.ti,kf.
59	(diagnos* adj3 (classif* or differenti* or predict* or rapid* or RT-PCR or rRT-PCR)).ab.
60	diagnostic test approval/ or diagnosis time/
61	laboratory diagnosis/
62	molecular diagnosis/

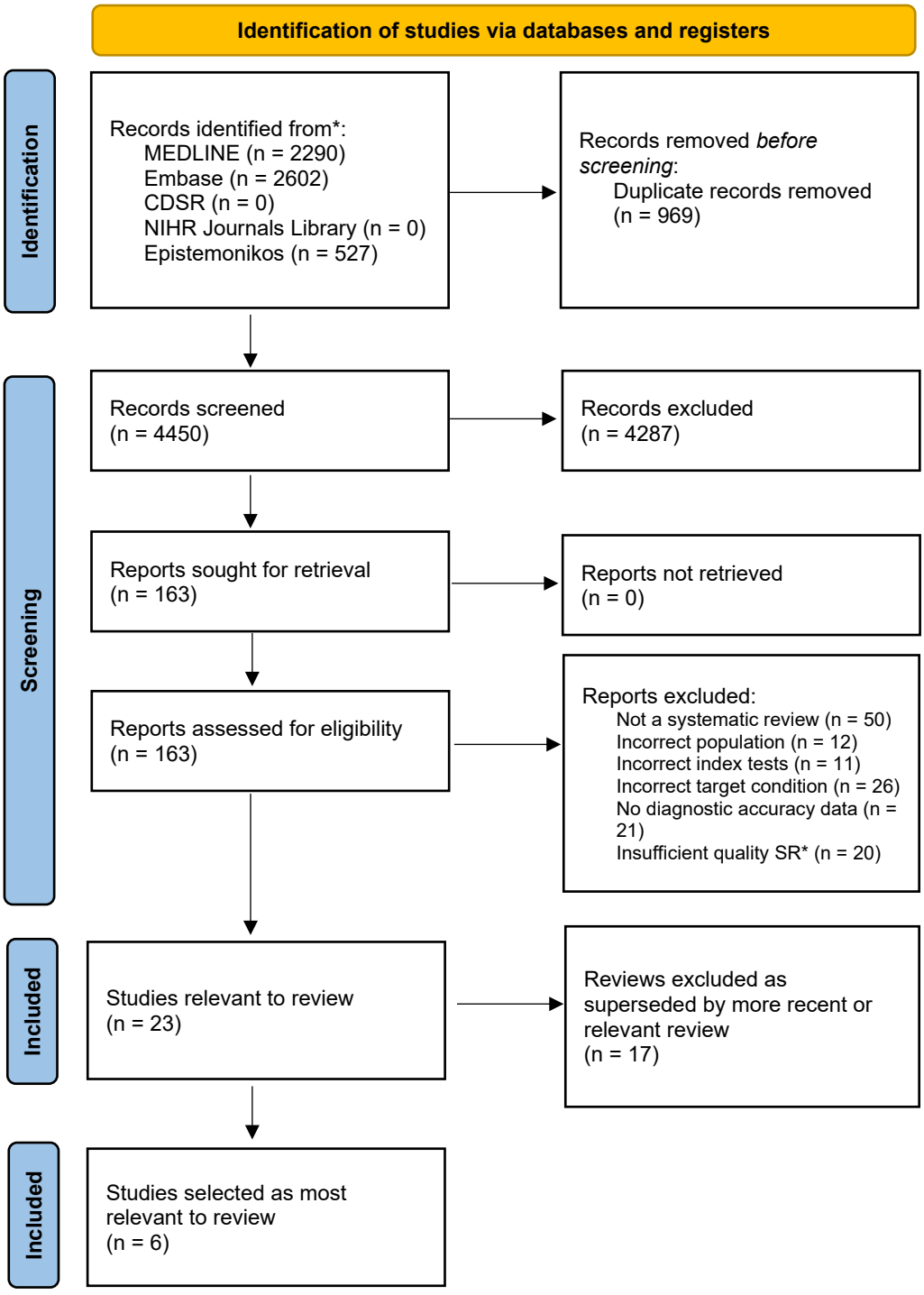
63	((accura* or reliab* or valid*) and (point-of-care or POC or (rapid adj2 (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*)))).tw,kf.
64	((accura* or reliab* or valid*) and (bacteri* and (viral or virus*) and (analys* or assay* or immunoassay* or classif* or detect* or diagnos* or differenti* or predict* or technique* or test*))).tw,kf.
65	"quality assessment of diagnostic accuracy studies"/
66	(QUADAS* or STARD).mp.
67	differential diagnosis/
68	(codetect* or co-detect* or codiagnos* or co-diagnos*).tw,kf.
69	((discriminat* or differenti* or dual*) adj (detect* or diagnos*)).mp.
70	(bacteri* adj5 (viral or virus*) adj5 (analys* or assay* or immunoassay* or classif* or detect* or codetect* or determin* or diagnos* or codiagnos* or differenti* or discriminat* or distinguish* or identif* or method* or misdiagnos* or predict* or kit or kits or panel? or predict* or rapid or routine* or screen* or system* or technique* or test*)).tw,kf,hw.
71	"sample to answer".mp.
72	or/32-71
73	[Index Tests: Rapid Multiplex PCR]
74	rapid test/dc
75	(multiplex* and "sample to answer").mp.
76	(74 or 75) and 30
77	(maripoc* or mari-poc*).mp,ct,dv,dc,dm,mv,my,tn.
78	(Rapid* and Diagnostic* and (MiniLab* or mini-lab*)).mp,ct,dv,dc,dm,mv,my,tn.
79	(QIAstat* or QIA-stat* or (Qiagen* and (Resp* adj3 panel))).mp,ct,dv,dc,dm,mv,my,tn.
80	Biofire* Respiratory.mp,ct,dv,dc,dm,mv,my,tn.
81	BioFire* RP*.mp,ct,dv,dc,dm,mv,my,tn.
82	(Biofire* and "sample to answer").mp,ct,dv,dc,dm,mv,my,tn.
83	(Biofire* adj5 (rapid or real time or RT-PCR or rRT-PCR)).mp,ct,dv,dc,dm,mv,my,tn.
84	or/77-83
85	(BioFire* adj (FilmArray* or Film-Array) adj (Respiratory Panel? or RP*)).mp,ct,dv,dc,dm,mv,my,tn.
86	(Biofire* adj (FilmArray* or Film-Array*) adj Pneumonia).mp,ct,dv,dc,dm,mv,my,tn.
87	(85 or 86) and 72
88	(Biofire* adj (FilmArray* or Film-Array*)).ti.
89	88 and 30 and 72
90	(Spotfire* or Spot-fire*).mp,ct,dv,dc,dm,mv,my,tn.
91	90 and (30 or 72)
92	(Cobas* adj5 ((lab* adj3 tube*) or liat*)).mp,ct,dv,dc,dm,mv,my,tn.
93	(cobas* Influenza A* or cobas* Influenza B* or cobas* RSV or cobas* respiratory sync* virus).mp,ct,dv,dc,dm,mv,my,tn.
94	(92 and 30 and 72) or 93
95	(Xpert* adj3 Xpress* adj3 (influenza or flu or respiratory sync* virus or RSV)).mp,ct,dv,dc,dm,mv,my,tn.

96	(Cepheid* adj3 Xpert* adj3 (influenza or flu or respiratory sync* virus or RSV)).mp,ct,dv,dc,dm,mv,my,tn.
97	((Cepheid* adj3 GeneXpert* adj3 Xpress*) or (Cepheid* adj3 Gene-Xpert* adj3 Xpress*)).mp,ct,dv,dc,dm,mv,my,tn.
98	((95 or 96) and 72) or 97
99	(ePlex* RP* or (ePlex* adj3 resp* adj3 panel?)).mp,ct,dv,dc,dm,mv,my,tn.
100	ePlex*.mp,ct,dv,dc,dm,mv,my,tn.
101	(100 and 72) or 99
102	((GenMark* or Gen-Mark*) and (RP* or (resp* adj3 panel?))).mp,ct,dv,dc,dm,mv,my,tn.
103	102 and 72
104	76 or 84 or 87 or 89 or 91 or 94 or 98 or 101 or 103
105	(Simplexa* or Liaison* MDX*).mp,ct,dv,dc,dm,mv,my,tn.
106	105 and 30 and 72
107	Aries*.mp,ct,dv,dc,dm,mv,my,tn.
108	(sheep or lamb or lambs or ram or rams or ewe or ewes or ovine or ovis aries).ti.
109	107 not 108
110	109 and 30 and 72
111	(Savanna* and (quidel* or molecular or multiplex* or rapid or real-time or RTPCR or RT-PCR or rRTPCR or rRT-PCR or test? or device? or panel? or PoCT or Point-of-Care or near-patient?)).mp,ct,dv,dc,dm,mv,my,tn.
112	((RVP4* or RVP-4*) and (Savanna* or Quidel* or molecular or multiplex* or rapid or real-time or RTPCR or RT-PCR or rRTPCR or rRT-PCR or test? or device? or panel? or PoCT or Point-of-Care or near-patient?)).mp,ct,dv,dc,dm,mv,my,tn.
113	(respiratory vir* Panel4* or respiratory vir* Panel-4*).mp,ct,dv,dc,dm,mv,my,tn.
114	(111 or 112 or 113) and 30
115	Verigen*.mp,ct,dv,dc,dm,mv,my,tn.
116	115 and 30 and 72
117	Panther* Fusion*.mp,ct,dv,dc,dm,mv,my,tn.
118	117 and 30 and 72
119	Paraflu*.mp,ct,dv,dc,dm,mv,my,tn.
120	119 and 72
121	"Flu A/B/RSV*".mp,ct,dv,dc,dm,mv,my,tn.
122	"AdV/hMPV/RV*".mp,ct,dv,dc,dm,mv,my,tn.
123	106 or 110 or 114 or 116 or 118 or 120 or 121 or 122
124	104 or 123
125	((COVID19 or COVID-19 or COVID2019 or COVID-2019 or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2" or 2019 nCoV or 2019nCoV or 2019-novel CoV or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2") not (rhinovir* or rhino* vir* or coryzavir* or coryza* vir* or influenzavir* or influenza* vir* or (H1N1 or H3N2) or parainfluenzavir* or parainfluenza* vir* or pneumovir* or pneumo* vir* or human metapneumovir* or human meta-pneumovir* or HMPV or respiratory sync* vir* or RSV)).ti.
126	124 not 125

127	"SARS-CoV-2/Flu A/B*".mp,ct,dv,dc,dm,mv,my,tn.
128	"SARS-CoV-2/Flu A/B*".mp,ct,dv,dc,dm,mv,my,tn.
129	(("SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2" or "SARS coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2") adj3 Flu* adj3 RSV).mp,ct,dv,dc,dm,mv,my,tn.
130	or/126-129
131	((neonat* or infant* or child* or p?ediatri*) not adult*).ti.
132	130 not 131
133	limit 132 to conference abstract status
134	132 not 133

Appendix C –Diagnostic evidence study selection

Identification of relevant systematic reviews



* systematic review that searched only one database, or did not provide an assessment of methodological quality for included studies

Relevant systematic reviews

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
Bruning 2017	"…all available rapid tests for the detection of respiratory viruses in patients of all ages with RTIs." "Studies were considered for inclusion if they were written in English or Dutch and reported original data regarding the accuracy of a rapid	Medline and Embase	QUADAS-2	Jan 2016	179	Any rapid test	RSV	2	Adults and children	Not stated	Not stated	Both studies for RSV in mixed population. Excluded, as data superseded by more recent reviews (Gentilotti 2022 and Onwuchekwa 2023)
						Any rapid test	Influenza A and/or B	11	Adults	Not stated	Not stated	

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	test for ≥1 respiratory virus compared with PCR"											.
Carlton 2021	"Our review included diagnostic accuracy studies, reporting on point-of-care and rapid diagnostic tests consisting of more-than-one biomarker to identify bacterial or viral aetiology, in the general population presenting to	Medline, Embase, Web of Science	QUADAS-2	Feb 2021	20	Immuno-Xpert (TRAIL, IP-10 and CRP)	Bacterial or viral	4	Adults and children	Features of acute RTI	"the general population presenting to primary or secondary care…"	3 studies in adult/ mixed population. 3 in children/not reported. Included.
						FebriDx (CRP and MxA)	Bacterial or viral	4	Adults and children	Features of acute RTI	"the general population presenting	4 studies in adult/mixed population. 1 not reported.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	primary or secondary care with acute RTI symptoms."										to primary or secondary care…"	Included.
						CRP and neopterin	Bacterial or viral	1	Adults	Features of acute RTI	"the general population presenting to primary or secondary care…"	Included.
Chartrand 2012	"Studies were included if they assessed the accuracy of an	PubMed, EMBASE, BIOSIS and	QUADAS	Dec 2011	159	Any rapid test	Influenza A and/or B	17	Adults	Not stated	Not stated	Superseded by more recent review

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	RIDT [rapid influenza diagnostic test] against 1 of the 2 accepted reference standards. […] Acceptable reference standards included viral culture or RT-PCR"	Web of Science										(Gentilotti 2022).
Chartrand 2015	"Studies were considered for inclusion if they assessed the diagnostic accuracy of a commercial	PubMed and Embase	QUADAS-2	Apr 2015	71	Any rapid test	RSV	4	Adults	People with suspected ARI	Any setting	Not specific to primary/emergency care settings. Superseded

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	rapid immunoassay for RSV in patients with suspected ARI."											by more recent review (Onwuchekwa 2023).
Engel 2012	"Studies using adult patients (>16 years of age) consulting their GP with a probable LRTI were included if CRP was measured in (a part) of those patients."	Medline, Embase and the Cochrane Library	QUADAS and the 'Cochrane Validity Score'	July 2010	10	CRP	Bacterial LRTI and pneumonia	Narrative synthesis of 5 relevant articles.	Adults (>16 years).	Suspected LRTI. People with URTI/ confirmed pneumonia were excluded.	Primary care	No summary data are reported. Superseded by Gentilotti 2022.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
Falk 2008	"Population - participants in each study were to be recruited from a community, primary care setting or ambulatory setting, for example emergency departments, and have symptoms suggestive of acute respiratory infection suggestive of LRTI"	PubMed, EMBASE, Google Scholar, the Cochrane database and the MEDION database.	QUADAS	July 2008	8	CRP	Pneumonia	5-6 depending on threshold used	Adults (over 14 years)	ARI	Community and emergency care	Superseded by Gentilotti 2022.
Gentilotti 2022	"All the DTA studies […] on patients of any age were	PubMed, Web of Science, the Cochrane	QUADAS-2	May 2021	421	Symptoms and signs	Bacterial pneumonia	Between 4 and 26 studies,	Adults	Suspected LRTI	Community/emergen	Included.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	eligible for inclusion." Supplementary information: "A community-care setting was defined as the first point of contact with health services, including PC, LTCF, OC, and ER. POCT was defined as a test to support clinical decision making (signs and symptoms or imaging or host biomarkers or	Library, Embase and Open Gray						depending on symptoms/sign.			cy care settings	
						CRP	Pneumonia or bacterial pneumonia	4-6 (depending on threshold used)	Adults	Suspected LRTI	Community/emergency care settings	Included.
						Procalcitonin	Pneumonia or bacterial pneumonia	2-4 (depending on threshold used)	Adults	Suspected LRTI	Community/emergency care settings	Included.
						Immunochromatographic assay	Influenza A and/or B	15	Adults	Suspected LRTI	Community/emergen	Included.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	pathogen-based tests), which is performed on any part of the patient's body or clinical samples, during or close to the time of consultation."										cy care settings	
						Direct immunofluorescence	Influenza A and/or B	19	Mixed adults and children	Suspected LRTI	Community/emergency care settings	Included.
						Optical immunoassay	Influenza A and/or B	9	Mixed adults and children	Suspected LRTI	Community/emergency care settings	Included.
						Chemiluminescent neuraminidase assay	Influenza A and/or B	4	Mixed adults and children	Suspected LRTI	Community/emergency care settings	Included.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
						PCR based NAAT	Influenza A and/or B	6	Adults	Suspected LRTI	Community/emergency care settings	Included.
						Non-PCR based NAAT	Influenza A and/or B	2	Mixed adults and children	Suspected LRTI	Community/emergency care settings	Included.
						Rapid antigen detection test	RSV	35	Mixed adults and children	Suspected LRTI	Community/emergency care settings	Included.
						PCR based NAAT	RSV	38	Mixed adults and children	Suspected LRTI	Community/emergen	Included.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
											cy care settings	
						Non-PCR based NAAT	RSV	5	Mixed adults and children	Suspected LRTI	Community/emergency care settings	Included.
Hill 2019	Adult outpatients with acute cough due to suspected pneumonia.	PubMed, Scopus, and the Cochrane Library	QUADAS and DART	Mar 2017	Not stated	CRP	Pneumonia	Narrative synthesis of 6 articles	Adults	Suspected pneumonia	Not stated	Superseded by Gentilotti 2022
						Procalcitonin	Pneumonia	Narrative synthesis of 6 articles	Adults	Suspected pneumonia	Not stated	Superseded by Gentilotti 2022

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
						Symptoms and signs	Pneumonia	Narrative synthesis of 2 articles	Adults	Suspected pneumonia	Not stated	Superseded by Gentilotti 2022
Han 2020	Diagnostic test accuracy studies of lateral flow assays for influenza with at least 40 participants.	PubMed, Embase, Web of Science and the Cochrane Library	QUADAS-2	Nov 2019	13	Any lateral flow assay	Influenza A and/or B	13	Mixed adults and children	Not stated	Any	Superseded by Gentilotti 2022
Hoult 2022	"Cross-sectional, cohort and randomised controlled studies that describe associations	Embase and Medline	QUADAS-2	Mar 2018	39	CRP	Bacterial exacerbation of COPD	Narrative synthesis of 8 articles	Adults with COPD	Not stated.	Outpatient, hospitalised inpatients and ICU	Excluded as setting not sufficiently similar in scope to this review, and

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	between serum or sputum molecular or cellular biomarkers and evidence of bacterial infection in people with acute exacerbation of COPD were eligible for inclusion"											unable to extract relevant data.
						Procalcitonin	Bacterial exacerbation of COPD	Narrative synthesis of 5 articles	Adults with COPD	People with acute exacerbations of COPD.	Hospitalised inpatients and ICU	No studies relating to people attending primary/emergency care.
Htun 2019	"published studies that assessed clinical predictors of community-acquired pneumonia […].	PubMed, Embase, Cochrane Library	QUADAS-2	Mar 2018	13	Symptoms and signs	Pneumonia	Between 4 and 7 studies, depending on	Adults	Acute respiratory symptoms	Outpatient, primary or emergency care settings	Superseded by Gentilotti 2022

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	Studies were included if participants aged ≥18 years without serious illness (e.g. mechanical ventilation) and pre-existing immune suppression (HIV, malnutrition, and immunosuppressant medication)."							symptoms/sign.				
						CRP	Pneumonia	9	Adults	Acute respiratory symptoms	Outpatient, primary or emergency care settings	Superseded by Gentilotti 2022
						Procalcitonin	Pneumonia	4	Adults	Acute respiratory symptoms	Outpatient, primary or emergency care settings	Superseded by Gentilotti 2022

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
Huang 2018	"Studies that evaluated the performance of FDA-approved mPCR systems for the detection of viral respiratory infection were included, as follow: (a) they assessed the accuracy of one or more the following systems: FilmArray, Nanosphere Verigene RV+ and Hologic Gen-Probe Prodesse assays	PubMed, Embase	QUADAS-2	Jul 2017	20	Multiplex PCR	Multiple single pathogens	22 (influenza A) 13 (influenza B) 13 (RSV) 8 (adenovirus) 8 (hMPV)	Adults and children	Mixture of sympto matic people and stored samples	Not stated.	Scope to narrow for inclusion. Review limited to 2 rapid multiplex tests (and one laboratory based multiplex test).

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	[…] against reference standards…											
Lee 2021	"studies that evaluated the performance of the Quidel Sofia rapid influenza FIA, compared to a reference standard […] studies that included patients with influenza-like illness…"	Medline, Embase and the Cochrane Central Register	QUADAS-2	July 2020	17	Quidel Sofia rapid influenza fluorescent immunoassay	Influenza A and B	2 (influenza A) 1 (influenza B)	Adults	People with influenza-like illness	Not stated	Scope too narrow. Superseded by Gentilotti 2022

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
Merckx 2017	"…studies […] on the diagnostic accuracy of rapid influenza tests against an RT-PCR reference standard. Eligible participants were children and adults with clinically suspected influenza during periods of influenza activity."	PubMed, Embase, BIOSIS Previews, Scopus, Web of Science and the Cochrane Central Register	QUADAS-2	May 2017	162	Traditional RIDT	Influenza A and B	23 (influenza A) 5 (influenza B)	Adults	Clinically suspected influenza	Mixed primary, emergency and hospital settings.	Superseded by Gentilotti 2022
						DIA	Influenza A and B	8 (influenza A) 7 (influenza B)	Adults	Clinically suspected influenza	Mixed primary, emergency and hospital settings.	Superseded by Gentilotti 2022
						Rapid NAAT	Influenza A and B	4 (influenza A)	Adults	Clinically suspected	Mixed primary, emergency and	Superseded by Gentilotti 2022

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
								4 (influenza B)		influenza	hospital settings.	
Minnaard 2017	"All studies on diagnostic accuracy of CRP for pneumonia (e.g., infiltrate on chest radiography as the reference standard) were eligible. Study participants had to be adults (≥ 18yr) suspected by their physician of having a lower respiratory tract infection presenting in a	Medline, Embase, the Cochrane Library	QUADAS-2	Not stated. Most recent included study published in 2013.	8	CRP and signs and symptoms	Pneumonia	8	Adults	Suspected LRTI	Primary and emergency care.	Included.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	primary health care setting…"											
Nicholson 2014	"…publications on influenza POCT diagnostic accuracy studies between 1991 and 2011 (inclusive) that met the following five criteria:1. Articles written in English.2. Commercially available test kits.3. Testing done in human seasonal and pandemic influenza…"	Medline, BIOSIS and the Cochrane Library	QUADAS and STARD	May 2011	70	Any POCT for influenza	Influenza	43	Mixed adults and children	Not stated	Not stated	Superseded by Gentilotti 2022

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
Onwuchekwa 2023	"primary studies were eligible if they reported on the diagnostic test performance or compared RSV detection rates using different specimens. We excluded […] studies in children, and in vitro studies."	Embase, Medline, Web of Science	QUADAS-2	Dec 2021	156	DFA	RSV	1	Adults	Acute exacerbation of asthma	Any setting	Included.
						RADT	RSV	1	Adults	LRTI and URTI	Any setting	Included.
						Multiplex PCR	RSV	1	Adults	LRTI and URTI	Any setting	Excluded, as new review of multiplex tests was conducted.
Pazmany 2021	": a) adult patients with bacterial and non-bacterial	Medline, Embase, CENTRAL,	QUADAS-2	Oct 2019	21	Symptoms and signs	Bacterial acute	3	Adults	Acute exacerb	Any setting	Includes predominantly primary

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	AECOPD; b) results of microbiology tests (as the reference standard) with samples taken from sputum, tracheal aspirates or blood; and c) at least one other on-admission diagnostic test performed from serum or sputum(index tests), were considered eligible"	Scopus and Web of Science				(sputum colour only)	exacerbation of COPD			ation of COPD		care setting. Included.
						CRP	Bacterial acute exacerbation of COPD	9	Adults	Acute exacerbation of COPD	Any setting	All relate to hospitalised participants. Not sufficiently close in scope to this review question (no data relating to outpatient/primary/emerg
						Procalcitonin	Bacterial acute exacerbation of COPD	8	Adults	Acute exacerbation of COPD	Any setting	
						Neutrophil/lymphocyte ratio	Bacterial acute exacerbation of COPD	1	Adults	Acute exacerbation of COPD	Any setting	

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
						Eosinophil %	Bacterial acute exacerbation of COPD	1	Adults	Acute exacerbation of COPD	Any setting	ency settings)
Petrozzino 2010	"Articles reporting RFT and clinical diagnostic performance, and effects on decision-making and diagnostic outcomes" Adults and children with influenza-like illness.	PubMed/MEDLINE; the Cochrane Library; British Medical Journal Clinical Evidence; Surveillance, Epidemiology and End Results; the World Health	US Preventive Services Task Force (USPSTF) evidence-based guidelines for internal validity of diagnostic	2009	16	QuickVue rapid flu test	Influenza A and B	5	Adults (>/=15 years)	People presenting with influenza-like illness	Any setting	Superseded by Gentilotti 2022
						Symptoms and signs (clinical assessment)	Influenza A and B	11	Adults (>/=15 years)	People presenting with influenza-like illness	Any setting	Outside the scope of the protocol: clinical symptoms and signs for

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
		Organization website, the Agency for Healthcare Research and Quality website;	accuracy studies									a specific pathogen, rather than bacterial/viral infection.
Schierenberg 2016	"Models eligible for inclusion were logistic regression models including S&S [signs and symptoms] for predicting the probability of pneumonia in primary care	PubMed, Embase and the Cochrane Library	QUADAS-2	Aug 2012	8	Any clinical prediction rule for pneumonia (signs and symptoms)	Pneumonia	8	Adults	Acute or worsened cough or LRTI symptoms	Primary or emergency care	No summary estimates provided. Included.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	patients with acute cough or suspected LRTI"											
Van der Meer 2005	"We aimed to include studies that compared C reactive protein with a chest radiograph […] or microbiological work-up […]. We excluded articles concerning immunocompromised patients, patients treated in intensive care units,	Medline and Embase	Lijmer criteria	Apr 2004	17	CRP	Pneumonia	5	Adults	ARI	Primary/emergency care	Superseded by Gentilotti 2022

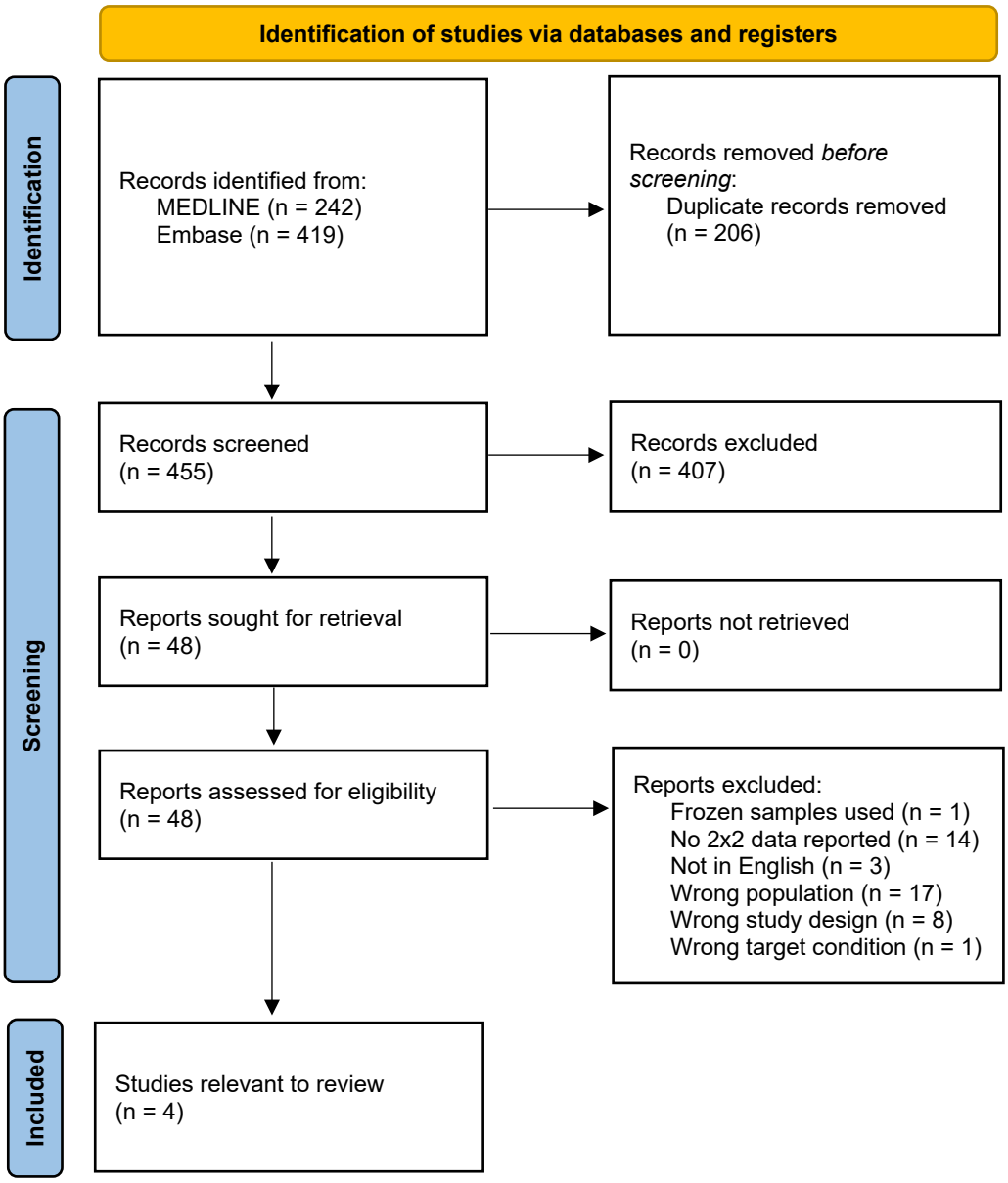
Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	or patients with hospital acquired pneumonia"											
Vos 2019	Supplementary material: "We included peer-reviewed studies in English or Dutch providing original data on the diagnostic accuracy or clinical impact of a molecular rapid test for respiratory viruses, among which at least influenza virus	Medline, Embase, Cochrane Library	QUADAS-2	Aug 2017	56	Any molecular rapid test	Influenza A and/or B and/or RSV (pooled estimate)	7	Adults	Mixed (some studies with symptoms of ARI, some not reported)	Not stated	Superseded by Gentilotti 2022.

Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	and/or RSV, as compared to (non-rapid) molecular techniques. […] The domain included patients of all ages with suspected (viral) RTI presenting in a hospital setting."											
Wu 2013	"articles [that provided an] evaluation of procalcitonin alone or compared with other laboratory markers, such as	Medline, EMBASE and the Cochrane Library	QUADAS	Nov 2011	6	Procalcitonin	Bacterial pneumonia	6	Adults	All diagnosed with H1N1 'flu	Predominantly ICU or inpatient	2 studies in emergency department or outpatient.

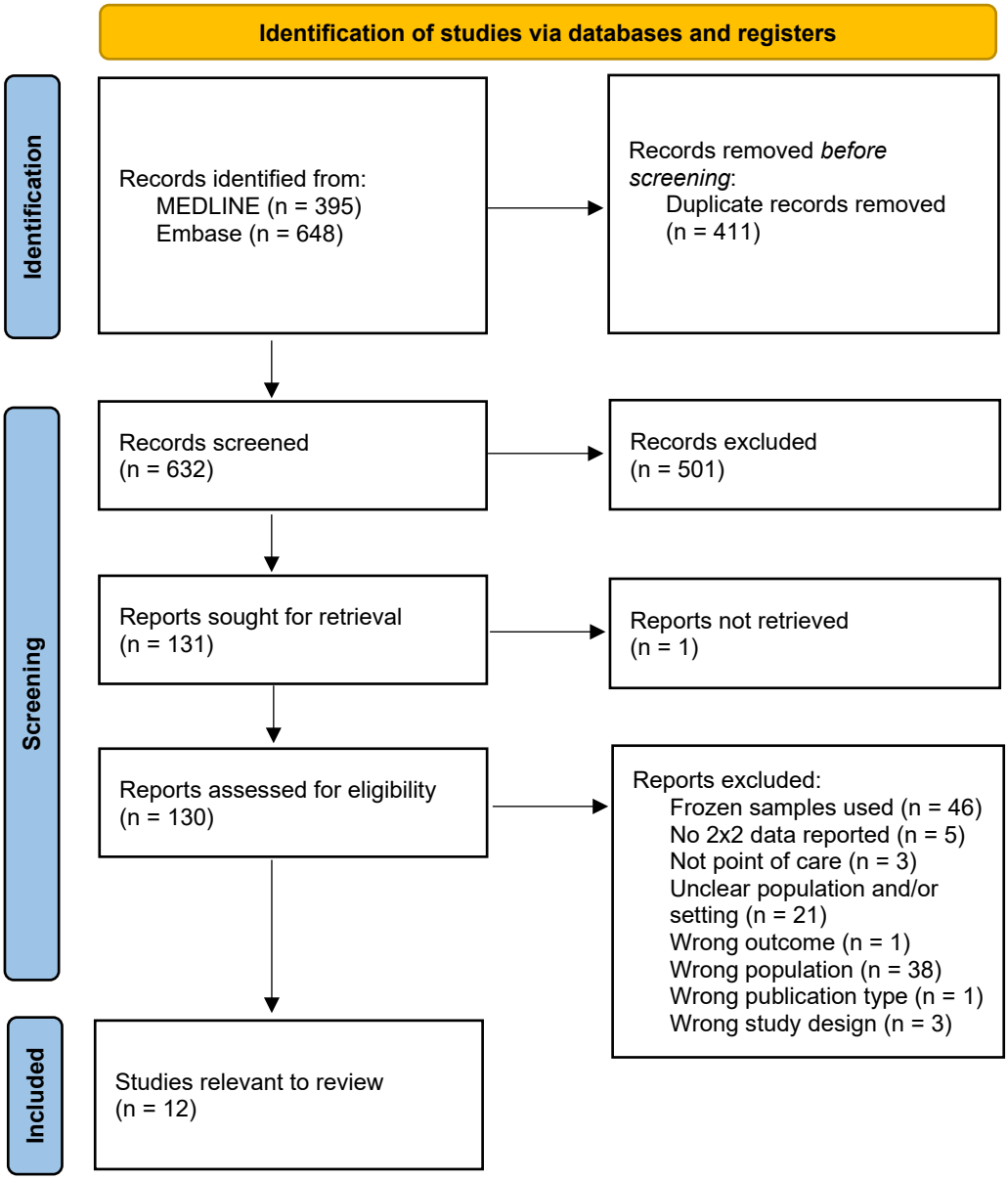
Reference	Eligibility criteria	Databases searched	Tool used to assess the validity of primary studies	Search date	Total number of studies included in the review	Index test	Target condition	Number of studies included in most relevant analysis	Population	Clinical features	Setting	Notes
	CRP, to diagnose bacterial pneumonia in patients with H1N1 influenza infection"											Superseded by Gentilotti 2022

ARI acute respiratory infection; CRP C-reactive protein; DART Documentation and Appraisal Review Tool; DFA direct fluorescence antibody; DIA digital immunoassay; hMPV human metapneumovirus; ICU intensive care unit; IP-10 interferon gamma induced protein 10; LRTI lower respiratory tract infection; NAAT nucleic acid amplification test; PCR polymerase chain reaction; POCT point of care test; QUADAS Quality Assessment of Diagnostic Accuracy Studies; RADT rapid antigen detection test; RFT rapid flu test; RIDT rapid influenza diagnostic test; RSV respiratory syncytial virus; TRAIL tumour necrosis factor-related apoptosis-inducing ligand; URTI upper respiratory tract infection

Identification of relevant primary studies for white blood cell count



Identification of relevant primary studies for multiplex tests



Appendix D –Diagnostic evidence

Evidence table 1: Included systematic reviews

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
Carlton 2021	This review included adults and children. Different analyses included different populations	People presenting with symptoms of acute respiratory tract infection.	Primary, emergency or secondary care.	Bacterial respiratory tract infection and viral respiratory tract infection	Combinations of biomarkers (at least 2 included).	Any reference standard. See details below for individual tests.	
	Adults and children	As above	Emergency department and inpatient	Bacterial and viral infection	TRAIL, IP-10 and CRP (ImmunoXpert)	Consensus of an expert panel	Sensitivity and specificity (and 95% confidence interval)
	Adults and children	As above	Emergency department and inpatient	Bacterial and viral infection	CRP and MxA (FebriDx)	Clinical algorithms and microbiology	

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
	Adults	As above	Emergency department and inpatient	Bacterial infection	CRP and neopterin	Clinical algorithm	
Gentilotti 2022	This review included adults and children. However, where possible we have extracted summary (subgroup) estimates which relate to adults only. See details provided for each index test.	Symptoms consistent with acute respiratory infection.	All included studies relating to primary/emergency care settings, including primary care, emergency department, outpatient clinics and long-term care facilities. Where possible we have extracted summary (subgroup) estimates to show the effect in these different settings. See details provided for each index test.	The target condition varied across the different index tests included. See details for each index test.	Symptoms and signs, host biomarkers (CRP and procalcitonin) and single pathogen tests for influenza. See individual tests listed below.	Any reference standard was permitted. See details below for individual tests.	

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
	Adults	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency	Bacterial pneumonia	Symptoms and signs, including: • Cough • Sputum production • Discoloured sputum • Chest pain • Dyspnoea • Sore throat • Runny nose • Myalgia • Chill • Diarrhoea • Impaired consciousness • SpO_2 • Fever >37.8^{0}C • Tachycardia • Tachypnoea • Reduced breath sounds • Wheezing • Crackles	Any reference standard, including the use of some/all of the following: X-ray, bacterial or viral culture, PCR, rapid antigen tests, lung ultrasound, composite analyses, expert opinion, microbiological diagnosis (not clarified), rapid influenza tests.	Pooled sensitivity and specificity estimates (with 95% CI) for each symptom.
	Adults	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency. Subgroup analysis for primary care only at one	Bacterial pneumonia	CRP	Any reference standard, including the use of some/all of the following: X-ray, bacterial or viral culture, PCR, rapid antigen tests, lung	Pooled sensitivity and specificity estimates (with 95% confidence interval) for

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
			measurement threshold (20mg/L)			ultrasound, composite analyses, expert opinion, microbiological diagnosis (not clarified), rapid influenza tests.	different thresholds of CRP.
	Adults for most analyses. Analysis at highest threshold (>0.50mcg/mL) includes adults and children, due to sparse data.	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency.	Bacterial pneumonia	Procalcitonin	Any reference standard, including the use of some/all of the following: X-ray, bacterial or viral culture, PCR, rapid antigen tests, lung ultrasound, composite analyses, expert opinion, microbiological diagnosis (not clarified), rapid influenza tests.	Pooled sensitivity and specificity estimates (with 95% confidence interval) for different thresholds of procalcitonin.

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
	Adults for main analysis. Subgroup analyses according to setting includes adults and children.	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency for main analysis. Also subgroup analyses for primary care, emergency department and outpatient clinic	Influenza	Immunochromatographic tests	Viral culture, PCR, antigen detection techniques and others	Pooled sensitivity and specificity estimates (with 95% confidence interval).
	Adults and children	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency for main analysis. Also subgroup analysis for emergency department only.	Influenza	Direct immunofluorescence	Viral culture, PCR, antigen detection techniques and others	Pooled sensitivity and specificity estimates (with 95% confidence interval).
	Adults and children	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency.	Influenza	Optical immunoassay	Viral culture, PCR, antigen detection techniques and others	Pooled sensitivity and specificity estimates (with 95% confidence interval).

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
	Adults and children	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency.	Influenza	MariPOC	Viral culture, PCR, antigen detection techniques and others	Pooled sensitivity and specificity estimates (with 95% confidence interval).
	Adults and children	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency.	Influenza	Chemiluminescent neuraminidase assay	Viral culture, PCR, antigen detection techniques and others	Pooled sensitivity and specificity estimates (with 95% confidence interval).
	Adults and children	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency.	Influenza	Nucleic acid amplification tests: standalone, single pathogen PCR	Viral culture, PCR, antigen detection techniques and others	Pooled sensitivity and specificity estimates (with 95% confidence interval).
	Adults and children	Symptoms consistent with acute respiratory infection.	Mixed primary and emergency for main analysis.	Influenza	Nucleic acid amplification tests: non-PCR based methods	Viral culture, PCR, antigen detection techniques and others	Pooled sensitivity and specificity estimates (with

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
			Subgroup analysis for emergency department only.				95% confidence interval).
Minnaard 2017	Adults	Suspected lower respiratory tract infection.	Primary health care, ambulatory care or emergency department settings.	Pneumonia	Combination of symptoms and signs plus CRP measurement.	Chest X-ray	Sensitivity and specificity estimates (with 95% confidence interval). The clinical prediction model and CRP level results in a 'predicted risk' for each participant. Sensitivity and specificity are then reported according to the use of different thresholds

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported
							of 'predicted risk' to identify people with pneumonia.
Onwuchekwa 2023	The review includes data on adults and children. We have extracted data which relate to adults only.	No information provided.	Primary care, emergency care and hospitalised participants.	RSV	Direct immunofluorescence and rapid antigen tests	RT PCR	Sensitivity and specificity estimates (with 95% confidence interval).
Pazmany 2021	Adults with COPD	Presenting with an acute exacerbation of COPD.	Primary care, emergency care and hospitalised participants.	Bacterial acute exacerbation of COPD.	Presence of purulent sputum.	Microbiological culture.	Sensitivity and specificity (and 95% confidence intervals).
Schierenberg 2017	Adults	Immunocompetent adults who self-referred with an acute or worsened cough or lower respiratory tract infection.	Primary care, ambulatory care or emergency departments	Pneumonia	Combinations of symptoms and signs (clinical prediction models)	Chest X-ray, CT or MRI	Area under the curve (and 95% confidence interval) for individual clinical prediction models.

ROBIS assessment for included systematic reviews

Review	Phase 2				Phase 3
	1. STUDY ELIGIBILITY CRITERIA	2. IDENTIFICATION AND SELECTION OF STUDIES	3. DATA COLLECTION AND STUDY APPRAISAL	4. SYNTHESIS AND FINDINGS	RISK OF BIAS IN THE REVIEW
Carlton 2021	☺	☺	☺	☺	☺
Gentilotti 2022	☺	☺	☺	☹	☺
Minnaard 2017	☺	☹	☺	☺	☺
Onwucheckwa 2023	☺	☺	☺	☺	☺
Pazmany 2021	☺	☺	☺	☺	☺
Schierenberg 2017	☺	☹	☺	☺	☺

☺Low Risk ☹High Risk ? Unclear Risk

Evidence table 2: White cell differential count, primary studies

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Outcomes reported	Funding/Conflicts of interest
Castro-Guardiola 2000	Adults (n = 284) 62% male. Mean age 57.2 years (standard deviation [SD] 20).	People who have been assessed by a clinician as having suspected pneumonia.	Emergency department, Spain.	Pneumonia	White blood cell count.	Typical findings on a chest X-ray, plus at least two of the following features: • Respiratory symptoms • Fever >38^{0}C • White cell count >12 million/ml • Microbiological confirmation	Area under the curve 0.65.	Not reported
Gulich 1999	Adults (n = 179) 46.4% male. Mean age 34.3 years (SD 13.4).	People presenting with a sore throat.	Primary care, Germany.	Bacterial pharyngitis	White blood cell count.	Culture of group A or C beta-haemolytic streptococci, or *haemophilus influenzae*.	Area under the curve 0.68.	The study was supported by Bundesverband der Betriebskrankenkassen and by Nycomed GmbH, Munich

Holm 2007	Adults (n = 364) 47% male. Median age 50 years.	People with symptoms of a lower respiratory tract infection.	Primary care, Denmark.	Pneumonia	White cell count ≥10 million/ml	Chest X-ray	Sensitivity 46% and specificity 80% (no confidence intervals reported)	Financial support received from the various contributors, including: The Danish Lung Association, The Danish Medical Research Association, and the Institute of Clinical Research. The authors declare no conflicts of interest
Liu 2013	Adults (n = 500) 58% male. Mean age 42.7 years (range 18 to 94).	People with a diagnosis of community acquired pneumonia, based on findings from a chest X-ray and symptoms.	Outpatient, China.	Bacterial pneumonia	White cell count <4 million/ml, 4-10 million/ml or >10 million/ml	Microbiological culture and PCR	2x2 data, sufficient to calculate sensitivity and specificity to diagnose bacterial infection at different thresholds of	Supported by grants from Beijing Science and Technology Key Projects Foundation. The authors declare no conflicts of interest.

							white cell count. **<4 million/ml** Sensitivity 10.07 (95% CI 5.74 to 16.06) Specificity 94.59 (95% CI 91.68 to 96.71) **4-10 million/ml** Sensitivity 71.14 (95% CI 63.16 to 78.26) Specificity 31.34 (95% CI 26.52 to 36.48) **>10 million/ml**	

							Sensitivity 18.79 (95% CI 12.87 to 26) Specificity 74.07 (95% CI 69.16 to 78.58)	

QUADAS-2 assessment, white cell differential count

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Castro-Guardiola 2000	☺	☺	☹	☺	☺	☹	☺
Gulich 1999	☺	☺	☺	☺	☺	☹	☺
Holm 2007	☹	☹	☺	☹	☺	☹	☺
Lui 2013	?	?	☺	☺	☺	☹	☺

☺ Low Risk ☹ High Risk ? Unclear Risk

Evidence table 3: Multiplex tests, primary studies

Reference	Population	Clinical features	Setting	Target condition assessed	Index tests	Reference standard	Notes	Funding/Conflicts of interest
Boku 2013	Adults. Mean age 34.4 years (range 20-63) 53.1% male.	Symptoms of acute respiratory infection, or presence of fever and known contact with influenza.	Hospital outpatient setting, Japan.	Flu A/B	Verigene system RV+ on nasopharyngeal swabs.	Viral culture plus laboratory PCR.		Not reported
Escarate 2022	Adults. Aged ≥ 65 years. Sex not reported.	Tested due to an outbreak of a respiratory illness. Symptoms of acute respiratory infection.	Outpatient/primary care (long-term care facilities), Australia.	Flu A, Flu B and RSV	Xpert Xpress Flu/RSV on nasopharyngeal swabs or combined nose and throat swabs.	Primary reference standard: PCR from central laboratory. Secondary reference standard: included expert opinion assessment of	Note that data are not included in the meta-analysis, as the authors only report specificity (not sensitivity) and the bivariate model requires both parameters.	The authors declare no conflicts of interest

						discordant specimens.		
Farfour 2022	Adults. Age not reported. Sex not reported.	Suspected viral respiratory infection.	Emergency department, France.	Flu A, RSV	Idylla SARS CoV/Flu/RSV on nasopharyngeal swabs.	Laboratory based multiplex PCR.		No external funding received
Hansen 2018	Adults and children (children comprised 20% of total population). Age not reported. Sex not reported.	Presenting with at least one sign of influenza.	Emergency department, USA.	Flu A/B	Cobas Liat Influenza A/B assay on nasopharyngeal swabs.	Primary reference standard: PCR from central laboratory. Secondary reference standard: included analysis of discordant specimens with a second multiplex rapid test.		Partial funding for this study was provided by an unrestricted educational grant from Roche molecular to GTH and from the Minneapolis Medical Research

Maignan 2016	Adults. Median 70 years (interquartile range [IQR] 44 to 84). 51% male.	Presenting with fever and at least one sign of a respiratory tract infection.	Emergency department, France.	Flu A, Flu B, Flu A/B	Cobas Liat Influenza A/B assay on nasopharyngeal swabs.	Primary reference standard: PCR from central laboratory, with analysis of discordant results with Xpert Xpress Flu/RSV assay and results from the national influenza virus reference centre.		Partially funded by Roche Diagnostics. Roche Diagnostics had no access to the data and were not involved in the interpretation of the data or the writing of the manuscript.
Morris 2021	Adults and children included in the study. Data were extracted which relate to adults presenting only. Median 55 years (IQR 29 to 73).	Symptoms of acute respiratory infection.	Emergency department, respiratory admissions unit and bone marrow transplant unit were included in the study, UK. Extracted data relate to adults in an emergency	Flu A, RSV	Xpert Xpress Flu/RSV. Sample type unclear.	Primary reference standard: laboratory based PCR.		No funding required. The authors declare no conflicts of interest.

	44.7% male.		department setting only.					
Peretz 2020	Adults. Aged 18 to 97. 57% male.	People with suspected influenza.	Emergency department, Israel.	Flu A/B	Xpert Xpress Flu A/B and Simplexa Flu A/B and RSV on nasopharyngeal swabs.	Comparator: rapid antigen test.	Note that this study provides data on concordance between multiplex PCR and a rapid antigen test. However, as the rapid antigen test is not regarded as a reference standard by the authors, these data were not included in the analysis. **Comparison of Xpert Xpress Flu with Influ A+B K-SeT**	No funding required. The authors declare no conflicts of interest.

							rapid antigen test: Percentage positive agreement: 96.3% (87.3 to 99.6) Percentage negative agreement: 95.7% (90.2 to 98.6) **Comparison of Simplexa Flu A/B and RSV with Influ A+B K-SeT rapid antigen test:** Percentage positive agreement:	

							96.3% (87.3 to 99.6) Percentage negative agreement: 97.4% (92.5 to 99.5)	
Tanei 2014	Adults. Median 30.5 years, range 20-63. 42.7% male.	Symptoms of acute respiratory infection plus a fever of ≥37^{0}C	Outpatients in a hospital general medical department, Japan.	Flu A/B	Verigene RV+	Primary reference standard: rapid antigen test	Note that this study provides data on concordance between multiplex PCR and a rapid antigen test. However, as the rapid antigen test is not regarded as a reference standard by the authors, these data were not	This study was supported in part by a Grant-in-Aid from the MEXT (Ministry of Education, Culture, Sports, Science and Technology) Strategic Research Foundation Project for Private Universities. The authors declare

							included in the analysis. **Comparison of Verigene RV+ with RapidTesta FLU II rapid antigen test:** Percentage positive agreement: 95.6% (84.9 to 99.5) Percentage negative agreement:56.8% (39.5 to 72.9)	no conflicts of interest
Valentin 2019	Adults. Age not reported.	Adult patients suffering from acute febrile respiratory tract infection with at least one risk factor	Emergency department, Austria.	Flu A, Flu B, Flu A/B	Xpert Xpress Flu/RSV and Cobas Liat Influenza A/B assay on nasopharyngeal swabs.	Primary reference standard: laboratory based PCR.		Reagents used for the tests were partly supplied by Roche and Cepheid. No other funding

	Sex not reported.	for complications of seasonal influenza						was received. The authors declare no conflicts of interest
Yin 2022	Adults and children (23% of participants were children). Age not reported. 58% male.	Symptoms of acute respiratory infection.	Emergency department, Belgium.	Flu A, Flu B, RSV	Cobas Liat Influenza A/B assay on nasopharyngeal swabs.	Primary reference standard: composite of rapid antigen tests plus culture. Samples were considered positive if they were positive on at least 2 of the three tests used (including the index test).		Roche diagnostics supplied instruments and reagents needed for this study. No personal grants or funding was received by the authors for this study. The authors declare no conflicts of interest
Youngs 2019	Adults. Age not reported.	Suspected influenza.	Emergency department, UK.	Flu A, Flu B, Flu A/B	Cobas Liat Influenza A/B assay on throat swabs.	Primary reference standard: composite of laboratory based		The authors declare no conflicts of interest

	Sex not reported.					PCR method and an alternative multiplex test (Xpert Xpress flu/RSV). Secondary reference standard: as above, but including expert opinion.		
Zuurbier 2022	Adults. 45.9% male. Median age 75 years (IQR 67-80)	Symptoms of acute respiratory tract infection.	Home setting/primary care, Belgium, Netherlands and UK.	RSV	Xpert Xpress Flu/RSV on nasopharyngeal swabs.	Primary reference standard: laboratory based PCR.		RESCEU has received funding from the Innovative Medicines Initiative 2 Joint Undertaking. Several authors declare they received personal fees from Roche,

								GSK, and other pharmaceutical companies, outside the submitted work. Additionally, University Medical Centre Utrecht received funding from various pharmaceutical companies.

QUADAS-2 assessment, multiplex tests

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Boku 2013	?	☺	?	☺	☺	☺	☺
Escarte 2022	?	☺	☺	☹	☹	☺	☺
Farfour 2022	☺	?	☺	☹	☺	☺	☺
Hansen 2018	☹	☺	☺	☺	☺	☺	☺
Maignan 2016	☺	☺	☺	☺	☺	☺	☺
Morris 2021	☹	☺	☺	☺	☺	☺	☺
Peretz 2020	?	?	☹	☺	☺	☹	☺
Tanei 2014	☺	?	☹	☺	☺	☹	☺
Valentin 2019	☺	☺	☺	☹	☺	☹	☺
Yin 2022	?	☺	☹	☺	☺	☹	☺
Youngs 2019	☺	☺	☹	☹	☺	☺	☺
Zuurbier 2022	☺	☺	☺	☹	☹	☺	☺

☺ Low Risk ☹ High Risk ? Unclear Risk

Appendix E – Meta-analyses

Figure 1: Sensitivity and specificity of multiplex tests for RSV

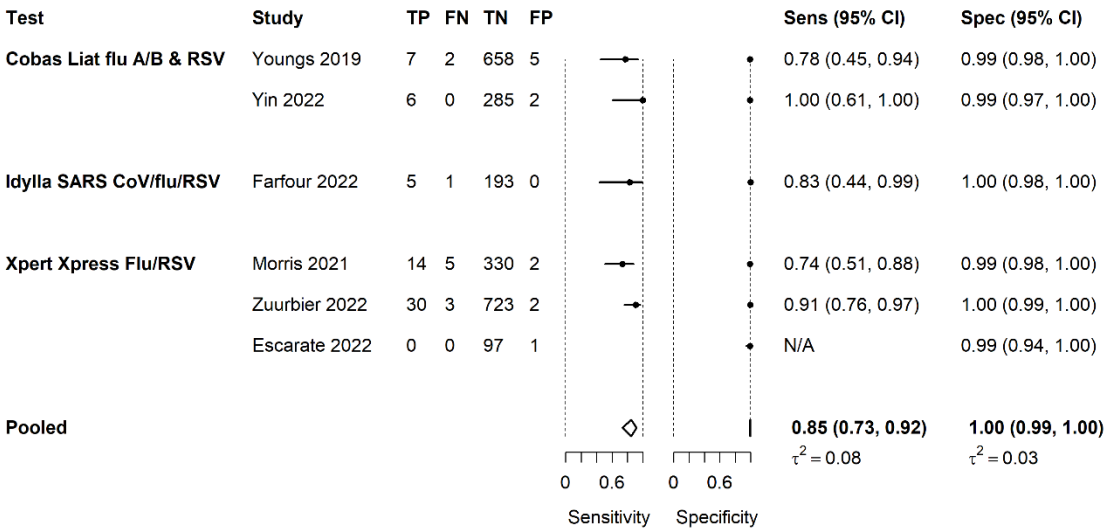


Figure 2: RSV data and overall meta-analysis results in ROC space

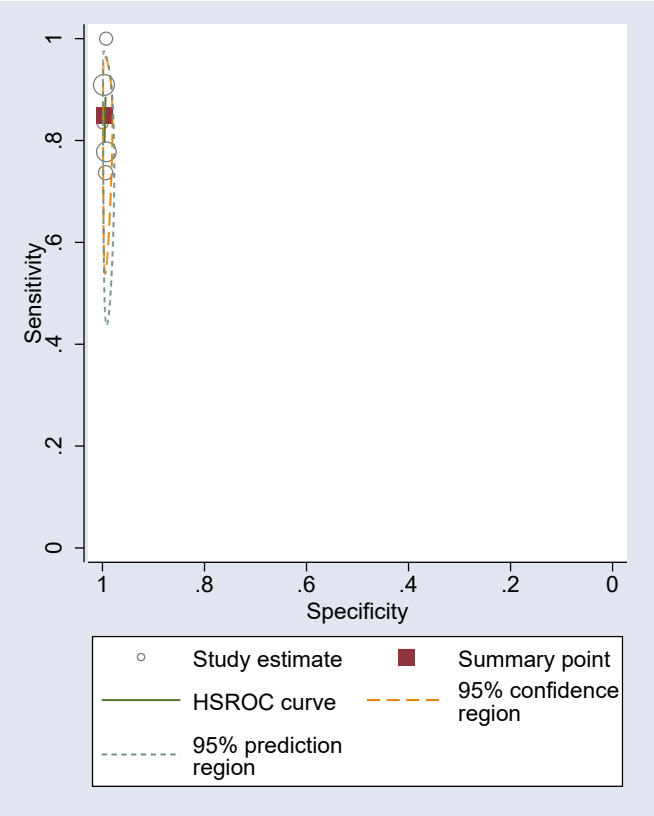


Figure 3: Sensitivity and specificity of multiplex tests for influenza A

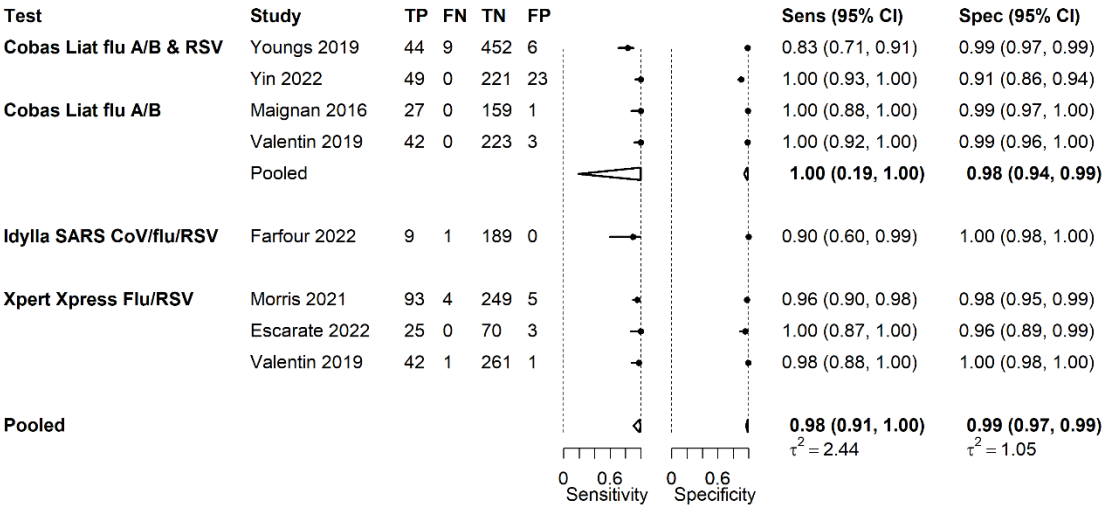


Figure 4: Influenza A data and meta-analysis results in ROC space

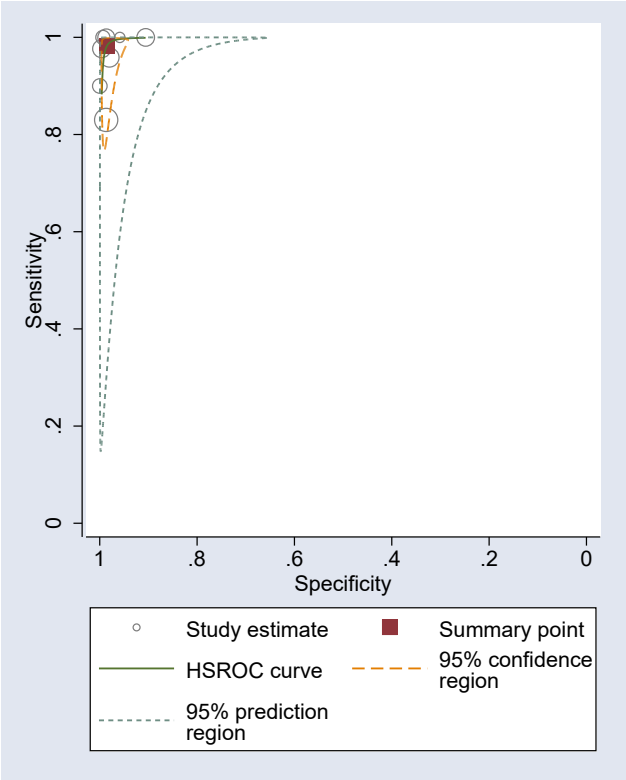


Figure 5: Sensitivity and specificity of multiplex tests for influenza B

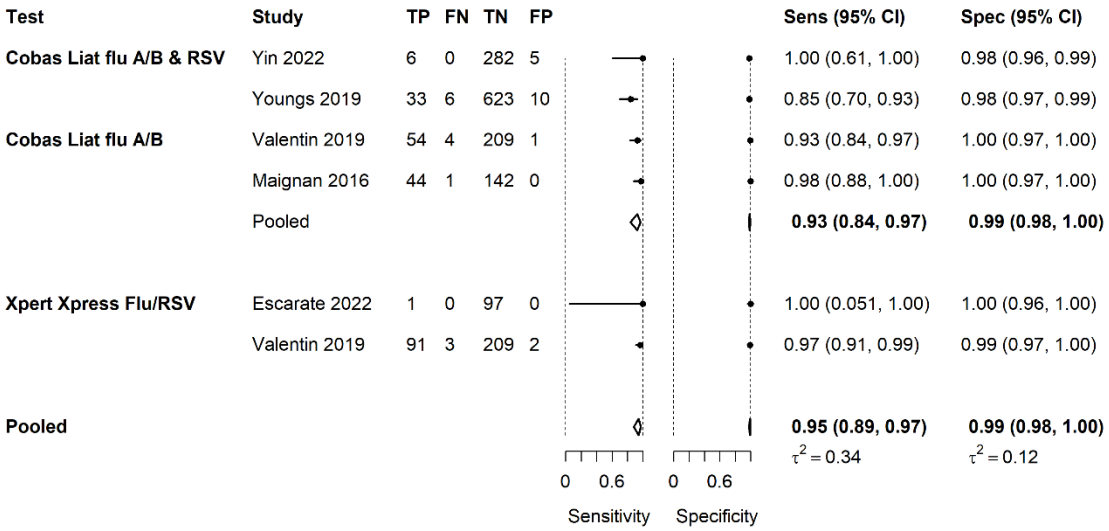


Figure 6: Influenza B data and meta-analysis results in ROC space

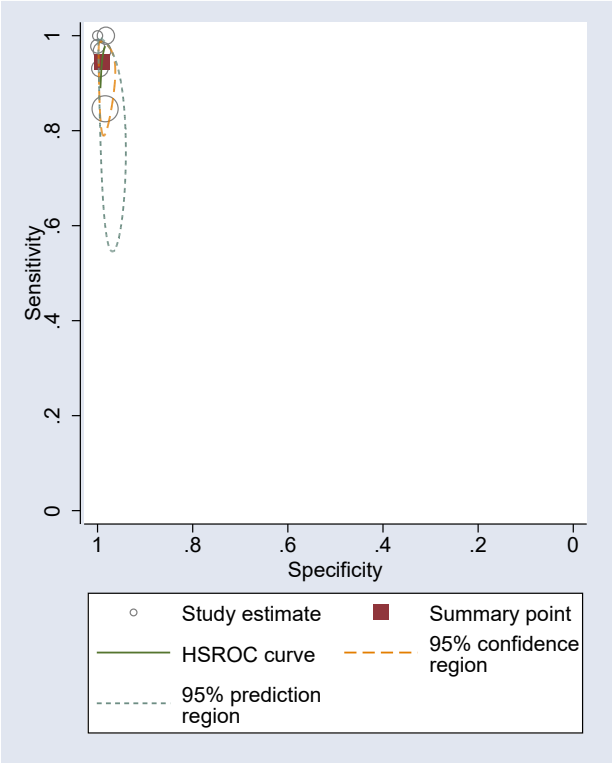


Figure 7: Sensitivity and specificity of multiplex tests for influenza A or B (combined)

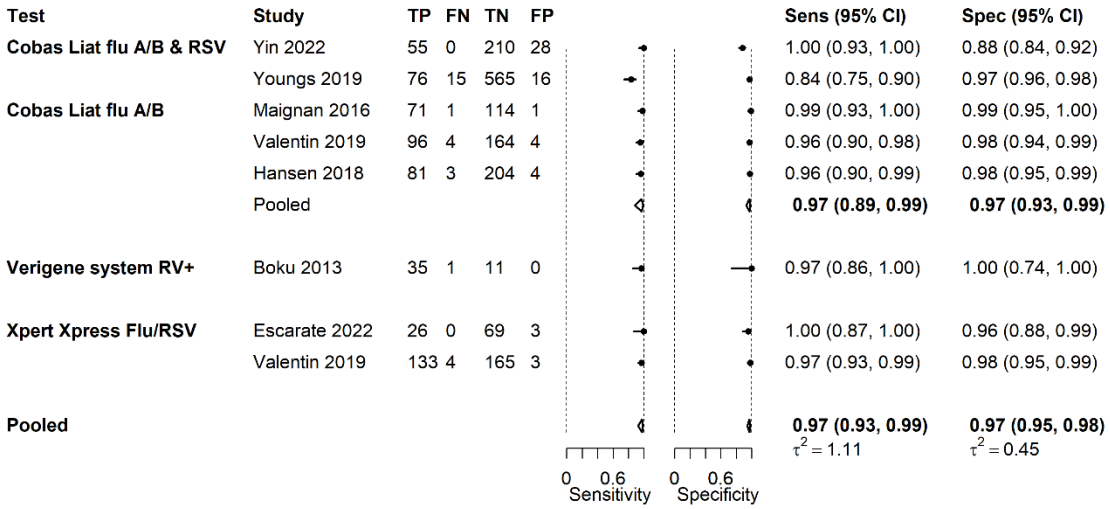
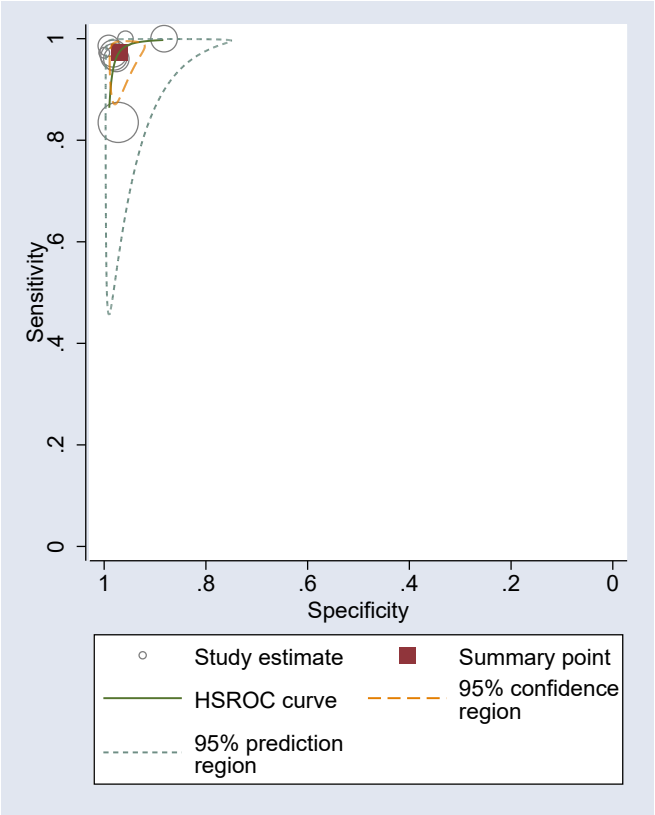


Figure 8: Influenza A and B data and meta-analysis results in ROC space



Appendix F – GRADE

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Signs and symptoms										
Cough	Gentilotti 2022	13 (8423)	Sensitivity	89.1% (66.4 to 97.1)	Serious[a]	Not serious[b]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
			Specificity	13.4% (2.5 to 48.4)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
Sputum production	Gentilotti 2022	7 (6392)	Sensitivity	63.9% (40.5 to 82.1)	Serious[a]	Not serious[b]	Unable to assess[c]	Serious[e]	Undetected	LOW
			Specificity	45.3% (25.9 to 66.3)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
Discoloured sputum	Gentilotti 2022	9 (3014)	Sensitivity	54.0% (39.8 to 67.7)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
			Specificity	53.0% (39.0 to 66.5)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
Purulent sputum (to detect bacterial exacerbations in people with COPD)	Pazmany 2021	3 (259)	Sensitivity	71% (42 to 90)	Serious[f]	No serious	Not serious	Very serious[d]	Undetected	VERY LOW
			Specificity	51% (30 to 73)	Serious[f]	No serious	Not serious	Not serious	Undetected	MODERATE
Chest pain	Gentilotti 2022	15 (8161)	Sensitivity	33.9% (21.5 to 49.0)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	73.0% (61.7 to 81.9)	Serious[a]	Not serious[b]	Unable to assess[c]	Serious[e]	Undetected	LOW
Dyspnoea	Gentilotti 2022	14 (6215)	Sensitivity	62.6% (53.3 to 71.1)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	45.5% (32.1 to 59.5)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Sore throat	Gentilotti 2022	5 (1096)	Sensitivity	32.6% (20.2 to 48.0)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	45.1% (33.1 to 57.6)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
Runny nose	Gentilotti 2022	7 (4630)	Sensitivity	45.3% (37.3 to 53.4)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	41.8% (28.1 to 56.8)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
Myalgia	Gentilotti 2022	6 (1430)	Sensitivity	41.6% (19.0 to 68.5)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	61.2% (40.7 to 78.4)	Serious[a]	Not serious[b]	Unable to assess[c]	Serious[e]	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Chill	Gentilotti 2022	8 (1933)	Sensitivity	45.7% (31.5 to 60.8)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	60.2% (48.5 to 70.8)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
Diarrhoea	Gentilotti 2022	5 (4268)	Sensitivity	10.8% (6.3 to 17.7)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	89.5% (75.4 to 95.9)	Serious[a]	Not serious[b]	Unable to assess[c]	Serious[e]	Undetected	LOW
Impaired consciousness	Gentilotti 2022	4 (3208)	Sensitivity	11.7% (9.3 to 14.5)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	92.9% (90.5 to 94.7)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
$Sp0_2$	Gentilotti 2022	6 (2821)	Sensitivity	22.8% (12.4 to 38.2)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	86.6% (80.7 to 90.9)	Serious[a]	Not serious[b]	Unable to assess[c]	Serious[e]	Undetected	LOW
Fever >37.8^{0}C	Gentilotti 2022	17 (11219)	Sensitivity	42.0% (26.7 to 58.9)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	80.4% (59.8 to 91.9)	Serious[a]	Not serious[b]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
Systolic BP	Gentilotti 2022	4 (3262)	Sensitivity	9.6% (2.8 to 28.3)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	95.0% (80.7 to 98.8)	Serious[a]	Not serious[b]	Unable to assess[c]	Serious[e]	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Tachycardia	Gentilotti 2022	11 (9474)	Sensitivity	27.2% (15.1 to 43.9)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	84.2% (71.5 to 91.9)	Serious[a]	Not serious[b]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
Tachypnoea	Gentilotti 2022	12 (10351)	Sensitivity	27.9% (13.1 to 49.8)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	80.2% (58.2 to 92.2)	Serious[a]	Not serious[b]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
Reduced breath sounds	Gentilotti 2022	4 (459)	Sensitivity	24.7% (8.3 to 54.4)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	89.0% (75.0 to 95.6)	Serious[a]	Not serious[b]	Unable to assess[c]	Serious[e]	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Wheezing	Gentilotti 2022	6 (2403)	Sensitivity	17.3% (9.6 to 29.2)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	86.4% (70.5 to 94.4)	Serious[a]	Not serious[b]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
Crackles	Gentilotti 2022	10 (6175)	Sensitivity	40.3% (23.6 to 59.7)	Serious[a]	Not serious[b]	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	83.1% (58.5 to 94.5)	Serious[a]	Not serious[b]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
Combinations of signs and symptoms										
Presence/absence of specific symptoms and signs	Schierenberg 2017	6 (not reported)	Area under the curve	Ranged from 53% to 79% depending on model used	Not serious	Not serious	Serious[g]	Serious [e]	Serious[h]	VERY LOW
Symptoms, signs and CRP										

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Predicted risk threshold 2.5%	Minnaard 2017	8 (5308)	Sensitivity	97% (95 to 98)	Not serious	Not serious	Unable to assess[c]	Not serious	Serious[h]	MODERATE
			Specificity	36% (34 to 37)	Not serious	Not serious	Unable to assess[c]	Not serious	Serious[h]	MODERATE
Predicted risk threshold 20%	Minnaard 2017	8 (5308)	Sensitivity	70% (66 to 73)	Not serious	Not serious	Unable to assess[c]	Not serious	Serious[h]	MODERATE
			Specificity	90% (89 to 91)	Not serious	Not serious	Unable to assess[c]	Serious[e]	Serious[h]	LOW
CRP										
CRP >10mg/L	Gentilotti 2022	4 (944)	Sensitivity	92% (56 to 99)	Serious[i]	Not serious	Unable to assess[c]	Very Serious[d]	Undetected	VERY LOW
			Specificity	43% (22 to 66)	Serious[i]	Not serious	Unable to assess[c]	Not serious	Undetected	MODERATE

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
CRP >20mg/L	Gentilotti 2022	5 (3531)	Sensitivity	83% (64 to 93)	Serious[i]	Not serious	Unable to assess[c]	Very Serious[d]	Undetected	VERY LOW
			Specificity	55% (37 to 73)	Serious[i]	Not serious	Unable to assess[c]	Not serious	Undetected	MODERATE
CRP >20mg/L (primary care only, adults and children)	Gentilotti 2022	4 (3362)	Sensitivity	78% (57 to 90)	Serious[i]	Serious[j]	Unable to assess[c]	Very Serious[d]	Undetected	VERY LOW
			Specificity	58% (36 to 78)	Serious[i]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW
CRP >50mg/L	Gentilotti 2022	5 (4219)	Sensitivity	77% (51 to 91)	Serious[i]	Not serious	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
			Specificity	74% (51 to 88)	Serious[i]	Not serious	Unable to assess[c]	Serious[e]	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
CRP >100mg/L	Gentilotti 2022	6 (4418)	Sensitivity	52% (31 to 72)	Serious[i]	Not serious	Unable to assess[c]	Not serious	Undetected	MODERATE
			Specificity	91% (79 to 97)	Serious[i]	Not serious	Unable to assess[c]	Serious[e]	Undetected	LOW
Procalcitonin										
Procalcitonin >0.1 mcg/mL	Gentilotti 2022	4 (1092)	Sensitivity	74% (38 to 93)	Serious[i]	Not serious	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
			Specificity	74% (36 to 94)	Serious[i]	Not serious	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
Procalcitonin >0.25 mcg/mL	Gentilotti 2022	5 (4019)	Sensitivity	44% (14 to 79)	Serious[i]	Not serious	Unable to assess[c]	Serious[e]	Undetected	LOW
			Specificity	89% (50 to 98)	Serious[i]	Not serious	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Procalcitonin >0.50 mcg/mL (adults and children)	Gentilotti 2022	4 (1195)	Sensitivity	44% (19 to 33)	Serious[i]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW
			Specificity	93% (43 to 100)	Serious[i]	Serious[j]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
TRAIL, IP-10 and CRP (ImmunoXpert)										
TRAIL, IP-10 and CRP to diagnose bacterial infection (adults and children)	Carlton 2021	4 (1291)	Sensitivity	85% (75 to 91)	Serious[k]	Serious[l]	Not serious	Serious[e]	Undetected	VERY LOW
			Specificity	86% (73 to 93)	Serious[k]	Serious[l]	Not serious	Very serious[d]	Undetected	VERY LOW
TRAIL, IP-10 and CRP to diagnose viral infection (adults and children)	Carlton 2021	3 (989)	Sensitivity	90% (79 to 96)	Serious[k]	Serious[l]	Serious[g]	Serious[e]	Undetected	VERY LOW
			Specificity	92% (83 to 96)	Serious[k]	Serious[l]	Not serious	Serious[e]	Undetected	VERY LOW
CRP and MxA (FebriDx)										

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
CRP and MxA to diagnose bacterial infection (adults and children)	Carlton 2021	4 (598)	Sensitivity	84% (75 to 90)	No serious	Serious[l]	No serious	Serious[e]	Undetected	LOW
			Specificity	93% (90 to 95)	No serious	Serious[l]	No serious	Not serious	Undetected	MODERATE
CRP and MxA to diagnose viral infection (adults and children)	Carlton 2021	4 (583)	Sensitivity	87% (72 to 95)	No serious	Serious[l]	No serious	Very serious[d]	Undetected	VERY LOW
			Specificity	82% (66 to 86)	No serious	Serious[l]	No serious	Serious[e]	Undetected	LOW
White cell differential count										
White cell count to diagnose pneumonia	Castro-Guardiola 2000, Holm 2007, Liu 2013	3 (1148)	2 studies reported sensitivity estimates ranging from 10.1 to 71.1%, and specificity estimates ranging from 31.3 to 94.6%, depending on the threshold used. 1 study reported an area under the curve of 0.65.		Serious[k]	Serious[m]	Serious[g]	Very serious[n]	Undetected	VERY LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
White cell count to diagnose bacterial pharyngitis	Gulich 1999	1 (179)	Area under the curve	0.68 (no confidence intervals)	No serious	Serious[m]	Not serious	Serious[o]	Undetected	LOW
Other host biomarkers										
CRP and neopterin to diagnose bacterial infection	Carlton 2021	1 (198)	Sensitivity	80% (71 to 86)	Serious[p]	Serious[q]	Not serious	Serious[e]	Undetected	VERY LOW
			Specificity	82% (71 to 89)	Serious[p]	Serious[q]	Not serious	Serious[e]	Undetected	VERY LOW
Single pathogen tests for influenza										
Immunochromatography	Gentilotti 2022	15 (2897)	Sensitivity	65% (47 to 79)	Serious[a]	Not serious	Unable to assess[c]	Serious[e]	Undetected	LOW
			Specificity	96% (92 to 98)	Serious[a]	Not serious	Unable to assess[c]	Not serious	Undetected	MODERATE
Immunochromatography (adults and children, primary care only)	Gentilotti 2022	11 (3351)	Sensitivity	56% (36 to 74)	Serious[a]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
			Specificity	95% (89 to 98)	Serious[a]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW
Immunochromatography (adults and children, emergency department only)	Gentilotti 2022	25 (15021)	Sensitivity	71% (60 to 80)	Not serious	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	LOW
			Specificity	98% (96 to 99)	Not serious	Serious[j]	Unable to assess[c]	Not serious	Undetected	MODERATE
Immunochromatography (adults and children, outpatient department only)	Gentilotti 2022	17 (6110)	Sensitivity	66% (55 to 76)	Not serious	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	LOW
			Specificity	97% (93 to 99)	Not serious	Serious[j]	Unable to assess[c]	Not serious	Undetected	MODERATE
Direct immunofluorescence	Gentilotti 2022	19 (7635)	Sensitivity	78% (67 to 86)	Serious[a]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
(adults and children)			Specificity	95% (90 to 98)	Serious[a]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW
Direct immunofluorescence (adults and children, emergency department only)	Gentilotti 2022	5 (1314)	Sensitivity	82% (72 to 89)	Serious[a]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW
			Specificity	96% (93 to 97)	Serious[a]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW
Optical immunoassay (adults and children)	Gentilotti 2022	9 (3910)	Sensitivity	68% (51 to 81)	Serious[a]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW
			Specificity	88% (81 to 93)	Serious[a]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW
MariPOC test (adults and children)	Gentilotti 2022	5 (1231)	Sensitivity	78% (61 to 89)	Serious[a]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
			Specificity	99% (97 to 99)	Serious[a]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW
Chemiluminescent neuraminidase assay (adults and children)	Gentilotti 2022	4 (787)	Sensitivity	81% (51 to 94)	Serious[a]	Serious[j]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
			Specificity	82% (65 to 91)	Serious[a]	Serious[j]	Unable to assess[c]	Very serious[d]	Undetected	VERY LOW
Nucleic acid amplification tests: standalone, single pathogen PCR (adults and children)	Gentilotti 2022	30 (25027)	Sensitivity	95.1% (89.3 to 97.8)	Serious[a]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW
			Specificity	97.5% (95.5 to 98.7)	Serious[a]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW
Nucleic acid amplification tests: non-PCR based	Gentilotti 2022	23 (4863)	Sensitivity	92% (88 to 94)	Serious[r]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
(adults and children)			Specificity	98% (95 to 99)	Serious[r]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW
Nucleic acid amplification tests: non-PCR based (adults and children, emergency department only)	Gentilotti 2022	14 (3138)	Sensitivity	91% (87 to 94)	Serious[r]	Serious[j]	Unable to assess[c]	Serious[e]	Undetected	VERY LOW
			Specificity	98% (95 to 99)	Serious[r]	Serious[j]	Unable to assess[c]	Not serious	Undetected	LOW
Single pathogen tests for RSV										
Direct immunofluorescence	Onwuchekwa 2023	1 (49)	Sensitivity	56% (31 to 78)	Not serious	Not serious	Serious[s]	Very serious[t]	Undetected	VERY LOW
			Specificity	100% (89 to 100)	Not serious	Not serious	Serious[s]	Very serious[t]	Undetected	VERY LOW
Rapid antigen test	Onwuchekwa 2023	1 (281)	Sensitivity	18% (12 to 27)	Serious[u]	Serious[v]	Not serious	Not serious	Undetected	LOW
			Specificity	98% (86 to 100)	Serious[u]	Serious[v]	Not serious	Serious[e]	Undetected	VERY LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
Multiplex tests										
All multiplex tests for RSV	Farfour 2022, Morris 2021, Yin 2022, Youngs 2019, Zuurbier 2022	5 studies (2273)	Sensitivity	84.9% (73.5 to 91.9)	Serious[k]	Not serious	Not serious	Very serious[d]	Undetected	VERY LOW
			Specificity	99.5% (99.1 to 99.7)	Serious[k]	Not serious	Not serious	Not serious	Undetected	MODERATE
Cobas Liat tests for RSV	Yin 2022, Youngs 2019	2 studies (965)	Sensitivity	86.7% (59.5 to 96.6)	Serious [k]	Not serious	Not serious	Very serious[d]	Undetected	VERY LOW
			Specificity	99.3% (98.5 to 99.6)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE
Xpert Xpress tests for RSV	Morris 2021, Zuurbier 2022	2 studies (1109)	Sensitivity	84.5% (69.4 to 92.9)	Serious [k]	Not serious	Not serious	Very serious[d]	Undetected	VERY LOW
			Specificity	99.6% (99.0 to 99.9)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE
All multiplex tests for influenza A	Escarate 2022, Farfour 2022, Morris 2021, Maignan	8 studies (2212)	Sensitivity	98.2% (90.7 to 99.7)	Serious [k]	Not serious	Serious[w]	Not serious	Undetected	LOW
			Specificity	98.6% (96.6 to 99.4)	Serious [k]	Not serious	Serious[w]	Not serious	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
	2016, Valentin 2019 (two tests included), Yin 2022, Youngs 2019.									
Cobas Liat tests for influenza A	Maignan 2016, Valentin 2019, Yin 2022, Youngs 2019.	4 studies (1259)	Sensitivity	99.8% (18.8 to 100)	Not serious	Not serious	Serious[w]	Very serious[d]	Undetected	VERY LOW
			Specificity	97.9 (94.0 to 99.3)	Not serious	Not serious	Serious[w]	Not serious	Undetected	MODERATE
Xpert Xpress tests for influenza A	Escarate 2022, Morris 2021, Valentin 2019.	3 studies (754)	Sensitivity	97.0% (92.9 to 98.7)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE
			Specificity	98.5% (96.2 to 99.4)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE
All multiplex tests for influenza B	Escarate 2022, Maignan 2016, Valentin 2019 (two tests included), Yin	6 studies (1823)	Sensitivity	94.5% (88.6 to 97.5)	Serious [k]	Not serious	Serious[w]	Serious[e]	Undetected	VERY LOW
			Specificity	99.1 (98.1 to 99.6)	Serious [k]	Not serious	Serious[w]	Not serious	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
	2022, Youngs 2019.									
Cobas Liat tests for influenza B	Maignan 2016, Valentin 2019, Yin 2022, Youngs 2019.	4 studies (1420)	Sensitivity	92.9% (84.3 to 96.9)	Not serious	Not serious	Serious[w]	Serious[e]	Undetected	LOW
			Specificity	99.0% (97.6 to 99.6)	Not serious	Not serious	Serious[w]	Not serious	Undetected	MODERATE
Xpert Xpress tests for influenza B	Escarate 2022, Valentin 2019.	2 studies (403)	Sensitivity	96.4% (90.7 to 99.0)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE
			Specificity	99.4% (97.4 to 99.8)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE
All multiplex tests for influenza A/B	Boku 2013, Escarate 2022, Hansen 2018, Maignan 2016, Valentin 2019 (two tests included), Yin	8 studies (2162)	Sensitivity	97.4% (92.9 to 99.0)	Serious [k]	Not serious	Serious[w]	Not serious	Undetected	LOW
			Specificity	97.0% (94.5 to 98.4)	Serious [k]	Not serious	Serious[w]	Not serious	Undetected	LOW

Index test	Source of data	No. of included studies (participants)	Outcome	Result (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Certainty of the body of evidence
	2022, Youngs 2019.									
Cobas Liat tests for influenza A/B	Hansen 2018, Maignan 2016, Valentin 2019, Yin 2022, Youngs 2019.	5 studies (1712)	Sensitivity	97.1% (88.6 to 99.3)	Not serious	Not serious	Serious[w]	Serious[e]	Undetected	LOW
			Specificity	96.8% (93.2 to 98.5)	Not serious	Not serious	Serious[w]	Not serious	Undetected	MODERATE
Xpert Xpress tests for influenza A/B	Escarate 2022, Valentin 2019	2 studies (403)	Sensitivity	97.5% (93.6 to 99.1)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE
			Specificity	97.5% (94.5 to 98.9)	Serious [k]	Not serious	Not serious	Not serious	Undetected	MODERATE

a Serious risk of bias as majority of studies included analyses had a high or unclear risk of bias in at least one QUADAS-2 domain.

b Rated as no serious risk of indirectness, as adults patients, attending primary, ambulatory or emergency care with symptoms of ARI. However, note that chest X-ray was used as the reference standard in many studies, which may not adequately distinguish between bacterial and viral pneumonia.

c No information on heterogeneity is provided, and no forest plots are available to assess inconsistency.

d Confidence interval crosses two decision thresholds (taken to be 90% and 75%)

e Confidence interval crosses one decision threshold (taken to be 90% and 75%)

f Two included studies at unclear risk of bias in patient selection, one included study at high risk and another at unclear risk of bias for patient flow and timing

g Confidence intervals for individual studies do not overlap.

h Studies were only included if the authors were able to provide original individual participant data. 4 studies were excluded, as the authors were unable to provide this, or did not reply to the request.

i Serious risk of bias as majority of studies included had an unclear risk of bias in at least one QUADAS-2 domain.

j Serious indirectness, as this analysis included adults and children.

k High or unclear risk of bias in at least one domain of every study. Majority of studies considered high risk of bias for at least one domain overall.

l Adults and children included in analysis. May include some participants who were hospitalised.

m All index tests were conducted in a laboratory setting, not using a POC device.

n Considerable variation in estimates from individual studies. Unable to provide a pooled estimate across studies, due to variety of results presented.

o Unable to assess imprecision as no confidence intervals were presented.

p Serious risk of bias in two QUADAS-2 domains.

q Serious indirectness, as samples were stored before analysis, and unclear whether neopterin can be measured at POC

r Serious risk of bias as majority of studies included analyses had a high or unclear risk of bias in at least one QUADAS-2 domain. Note that this was assessed across all included nucleic acid amplification tests in the review (not the specific tests included in this analysis) as we were unable to determine exactly which studies were included.

s Specific test used in this study unlikely to be suitable for a point of care setting.

t Confidence interval crosses one decision threshold, and number of participants included was extremely small

u Three QUADAS-2 domains were rated as unclear risk of bias

v Study included some retrospective (frozen) samples, and may have included hospitalised participants.

w Prediction region wide, with relatively large tau^2

Appendix G – Economic evidence study selection

No economic evidence was included in this review.

Appendix H – Economic evidence tables

No economic evidence was included in this review.

Appendix I – Health economic model

No original economic modelling was undertaken.

Appendix J – Excluded studies

Excluded systematic reviews

Aalbers J, O'Brien KK, Chan W-S, Falk GA, Teljeur C, Dimitrov BD, et al. Predicting streptococcal pharyngitis in adults in primary care: a systematic review of the diagnostic accuracy of symptoms and signs and validation of the Centor score. BMC medicine. 2011;9:67.	Incorrect target condition (group A streptococcus)
Abdullahi H, Elnahas A, Konje JC. Seasonal influenza during pregnancy. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2021;258:235-9.	Not a systematic review
Abel L, Dakin HA, Roberts N, Ashdown HF, Butler CC, Hayward G, et al. Is stratification testing for treatment of chronic obstructive pulmonary disease exacerbations cost-effective in primary care? an early cost-utility analysis. International Journal of Technology Assessment in Health Care. 2019;35(2):116-25.	Not a systematic review
Alzahrani SA, Al-Salamah MA, Al-Madani WH, Elbarbary MA. Systematic review and meta-analysis for the use of ultrasound versus radiology in diagnosing of pneumonia. Critical ultrasound journal. 2017;9(1):6.	Incorrect index test (imaging)
Anevlavis S, Bouros D. Community acquired bacterial pneumonia. Expert opinion on pharmacotherapy. 2010;11(3):361-74.	Not a systematic review
Anjay MA, Anoop P. Diagnostic utility of rapid immunochromatographic urine antigen testing in suspected pneumococcal infections. Archives of disease in childhood. 2008;93(7):628-31.	Not a systematic review
Anonymous. Evaluation of rapid influenza diagnostic tests for influenza A (H3N2)v virus and updated case count--United States, 2012. MMWR Morbidity and mortality weekly report. 2012;61(32):619-21.	Not a systematic review

Anonymous. Infectious Disease/CDC Update: Update on emerging infections: news from the Centers for Disease Control and Prevention. Evaluation of 11 commercially available rapid influenza diagnostic tests-United States, 2011-2012. Annals of emergency medicine. 2013;61(5):573-7.	Not a systematic review
Anonymous. Streptococcal Antigen Test for Pneumonia Detection: A Review of Clinical and Cost-Effectiveness and Guidelines. 2015.	Not a systematic review
Anonymous. Erratum: A systematic review of rapid diagnostic tests for influenza: considerations for the community pharmacist (Journal of the American Pharmacists Association (2017) 57(1) (13-19) (S1544319116308056) (10.1016/j.japh.2016.08.018)). Journal of the American Pharmacists Association. 2018;58(1):128.	Not a systematic review
Aquino A, Paschoalin VMF, Tessaro LLG, Raymundo-Pereira PA, Conte-Junior CA. Updating the use of nano-biosensors as promising devices for the diagnosis of coronavirus family members: A systematic review. Journal of pharmaceutical and biomedical analysis. 2022;211:114608.	Not a systematic review
Au-Yong A. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 2. C-reactive protein in the differential diagnosis of heart failure and chest infection. Emergency medicine journal : EMJ. 2009;26(1):58-9.	No quality assessment of included studies, and searches of a single database only.
Avni T, Bieber A, Green H, Steinmetz T, Leibovici L, Paul M. Diagnostic Accuracy of PCR Alone and Compared to Urinary Antigen Testing for Detection of Legionella spp.: a Systematic Review. Journal of clinical microbiology. 2016;54(2):401-11.	Incorrect target condition (Légionnaires disease)

Babin SM, Hsieh Y-H, Rothman RE, Gaydos CA. A meta-analysis of point-of-care laboratory tests in the diagnosis of novel 2009 swine-lineage pandemic influenza A (H1N1). Diagnostic microbiology and infectious disease. 2011;69(4):410-8.	No quality assessment of included studies.
Bach PB, Brown C, Gelfand SE, McCrory DC. Management of acute exacerbations of chronic obstructive pulmonary disease: a summary and appraisal of published evidence. Annals of internal medicine. 2001;134(7):600-20.	No data on diagnostic accuracy outcomes.
Baez AA, Cochon L, Nicolas JM. A Bayesian decision support sequential model for severity of illness predictors and intensive care admissions in pneumonia. BMC medical informatics and decision making. 2019;19(1):284.	Not a systematic review
Basile K, Kok J, Dwyer DE. Point-of-care diagnostics for respiratory viral infections. Expert review of molecular diagnostics. 2018;18(1):75-83.	Not a systematic review
Basnayake TL, Waterer GW. Rapid diagnostic tests for defining the cause of community-acquired pneumonia. Current opinion in infectious diseases. 2015;28(2):185-92.	Not a systematic review
Bassetti M, Russo A, Righi E, Dolso E, Merelli M, D'Aurizio F, et al. Role of procalcitonin in bacteremic patients and its potential use in predicting infection etiology. Expert review of anti-infective therapy. 2019;17(2):99-105.	Not a systematic review
Berg P, Lindhardt BO. The role of procalcitonin in adult patients with community-acquired pneumonia--a systematic review. Danish medical journal. 2012;59(3):A4357.	Not a systematic review
Bernstein DI, Mejias A, Rath B, Woods CW, Deeter JP. Summarizing Study Characteristics and Diagnostic Performance of Commercially Available Tests for Respiratory Syncytial Virus: A Scoping Literature	No quality assessment of included studies.

Review in the COVID-19 Era. The journal of applied laboratory medicine. 2023;8(2):353-71.	
Biserni GB, Scarpini S, Dondi A, Biagi C, Pierantoni L, Masetti R, et al. Potential Diagnostic and Prognostic Biomarkers for Adenovirus Respiratory Infection in Children and Young Adults. Viruses. 2021;13(9).	Not a systematic review
Bond C, Morgenstern J, Heitz C, Milne WK. Hot off the Press: Difficult to Breathe - It Could be Pneumonia. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2020.	Not a systematic review
Boulet LP. Future directions in the clinical management of cough: ACCP evidence-based clinical practice guidelines. Chest. 2006;129(1):287S-92S.	Not a systematic review
Boulware DR, Daley CL, Merrifield C, Hopewell PC, Janoff EN. Rapid diagnosis of pneumococcal pneumonia among HIV-infected adults with urine antigen detection. The Journal of infection. 2007;55(4):300-9.	Incorrect population (people living with HIV)
Brown PM, Schneeberger DL, Piedimonte G. Biomarkers of respiratory syncytial virus (RSV) infection: specific neutrophil and cytokine levels provide increased accuracy in predicting disease severity. Paediatric respiratory reviews. 2015;16(4):232-40.	Not a systematic review
Brusselle G, Pavord ID, Landis S, Pascoe S, Lettis S, Morjaria N, et al. Blood eosinophil levels as a biomarker in COPD. Respiratory Medicine. 2018;138:21-31.	Not a systematic review
Bryan C, Boren SA. The use and effectiveness of electronic clinical decision support tools in the ambulatory/primary care setting: A systematic review of the literature. Informatics in Primary Care. 2008;16(2):79-91.	No data on diagnostic accuracy outcomes.

Bustamante A, Vilar-Bergua A, Guettier S, Sanchez-Poblet J, Garcia-Berrocoso T, Giralt D, et al. C-reactive protein in the detection of post-stroke infections: systematic review and individual participant data analysis. Journal of Neurochemistry. 2017;141(2):305-14.	Incorrect population (people who experience an infection after a stroke).
Call SA, Vollenweider MA, Hornung CA, Simel DL, McKinney WP. Does this patient have influenza? JAMA. 2005;293(8):987-97.	Not a systematic review
Carratala J, Garcia-Vidal C. An update on Legionella. Current opinion in infectious diseases. 2010;23(2):152-7.	Not a systematic review
Chen K, Ahmed S, Sun C, Sheng Y-J, Wu G, Deng C-L, et al. Accuracy of Molecular Amplification Assays for Diagnosis of Staphylococcal Pneumonia: a Systematic Review and Meta-analysis. Journal of clinical microbiology. 2021;59(8):e0300320.	Incorrect index test (staphylococcal organisms).
Chen Y-WR, Leung JM, Sin DD. A Systematic Review of Diagnostic Biomarkers of COPD Exacerbation. PloS one. 2016;11(7):e0158843.	No data on diagnostic accuracy outcomes.
Choi JJ, McCarthy MW. The prognostic value of mid-regional pro-adrenomedullin in the evaluation of acute dyspnea. Expert Review of Molecular Diagnostics. 2018;18(2):147-53.	Not a systematic review
Christ-Crain M, Muller B. Biomarkers in respiratory tract infections: diagnostic guides to antibiotic prescription, prognostic markers and mediators. The European respiratory journal. 2007;30(3):556-73.	Not a systematic review
Chu H, Lofgren ET, Halloran ME, Kuan PF, Hudgens M, Cole SR. Performance of rapid influenza H1N1 diagnostic tests: a meta-analysis. Influenza and other respiratory viruses. 2012;6(2):80-6.	No quality assessment of

	included studies.
Cohen JF, Cohen R, Levy C, Thollot F, Benani M, Bidet P, et al. Selective testing strategies for diagnosing group A streptococcal infection in children with pharyngitis: a systematic review and prospective multicentre external validation study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2015;187(1):23-32.	Incorrect target condition (group A streptococcus)
Corneli HM. Rapid strep tests in the emergency department: an evidence-based approach. Pediatric emergency care. 2001;17(4):272-9.	Incorrect target condition (group A streptococcus)
Covert K, Bashore E, Edds M, Lewis PO. Utility of the respiratory viral panel as an antimicrobial stewardship tool. Journal of Clinical Pharmacy and Therapeutics. 2021;46(2):277-85.	No data on diagnostic accuracy outcomes.
Cristovam E, Almeida D, Caldeira D, Ferreira JJ, Marques T. Accuracy of diagnostic tests for Legionnaires' disease: a systematic review. Journal of medical microbiology. 2017;66(4):485-9.	Incorrect target condition (Légionnaires disease)
Cruciani M, Mengoli C. An Overview of Meta-analyses of Diagnostic Tests in Infectious Diseases. Infectious Disease Clinics of North America. 2009;23(2):225-67.	No data on diagnostic accuracy outcomes.
Dale AP, Marchello C, Ebell MH. Clinical gestalt to diagnose pneumonia, sinusitis, and pharyngitis: a meta-analysis. The British journal of general practice : the journal of the Royal College of General Practitioners. 2019;69(684):e444-e53.	Searches were not comprehensive (single database only).

Dilger AE, Peters AT, Wunderink RG, Tan BK, Kern RC, Conley DB, et al. Procalcitonin as a Biomarker in Rhinosinusitis: A Systematic Review. American journal of rhinology & allergy. 2019;33(2):103-12.	No data on diagnostic accuracy outcomes.
Dubois C, Smeesters PR, Refes Y, Levy C, Bidet P, Cohen R, et al. Diagnostic accuracy of rapid nucleic acid tests for group A streptococcal pharyngitis: systematic review and meta-analysis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2021;27(12):1736-45.	Incorrect target condition (group A streptococcus)
Ebell MH. Predicting pneumonia in adults with respiratory illness. American Family Physician. 2007;76(4):560.	Not a systematic review
Ebell MH, Afonso A. A systematic review of clinical decision rules for the diagnosis of influenza. Annals of family medicine. 2011;9(1):69-77.	Searches were not comprehensive (single database only).
Ebell MH, Bentivegna M, Cai X, Hulme C, Kearney M. Accuracy of Biomarkers for the Diagnosis of Adult Community-acquired Pneumonia: A Meta-analysis. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2020;27(3):195-206.	Searches were not comprehensive (single database only).
Ebell MH, Chupp H, Cai X, Bentivegna M, Kearney M. Accuracy of Signs and Symptoms for the Diagnosis of Community-acquired Pneumonia: A Meta-analysis. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2020;27(7):541-53.	Searches were not comprehensive (single database only).
Ebell MH, Marchello C, Callahan M. Clinical Diagnosis of Bordetella Pertussis Infection: A Systematic Review. Journal of the American Board of Family Medicine : JABFM. 2017;30(3):308-19.	Incorrect target condition

	(bordatella pertussis)
Ebell MH, McKay B, Dale A, Guilbault R, Ermias Y. Accuracy of Signs and Symptoms for the Diagnosis of Acute Rhinosinusitis and Acute Bacterial Rhinosinusitis. Annals of family medicine. 2019;17(2):164-72.	Incorrect target condition (rhinosinusitis)
Ebell MH, McKay B, Guilbault R, Ermias Y. Diagnosis of acute rhinosinusitis in primary care: a systematic review of test accuracy. The British journal of general practice : the journal of the Royal College of General Practitioners. 2016;66(650):e612-32.	Incorrect target condition (rhinosinusitis).
Ebell MH, Rahmatullah I, Cai X, Bentivegna M, Hulme C, Thompson M, et al. A Systematic Review of Clinical Prediction Rules for the Diagnosis of Influenza. Journal of the American Board of Family Medicine : JABFM. 2021;34(6):1123-40.	Incorrect target condition (clinical prediction rules for influenza, not for bacterial/viral infection).
Ebell MH, Smith MA, Barry HC, Ives K, Carey M. The rational clinical examination. Does this patient have strep throat? JAMA. 2000;284(22):2912-8.	Incorrect target condition (group A streptococcus).
Ebell MH, Walsh ME, Fahey T, Kearney M, Marchello C. Meta-analysis of Calibration, Discrimination, and Stratum-Specific Likelihood Ratios for the CRB-65 Score. Journal of general internal medicine. 2019;34(7):1304-13.	Prediction model for severity, not diagnosis.
Ebell MH, White LL, Casault T. A systematic review of the history and physical examination to diagnose influenza. The Journal of the American Board of Family Practice. 2004;17(1):1-5.	Searches were not comprehensive (single database only).

Fekete T. Review: In suspected influenza, some rapid tests have high sensitivity and high specificity for detecting infection. Annals of Internal Medicine. 2018;168(2):JC9.	Not a systematic review
Flynn MF, Kelly M, Dooley JSG. Nasopharyngeal Swabs vs. Nasal Aspirates for Respiratory Virus Detection: A Systematic Review. Pathogens (Basel, Switzerland). 2021;10(11).	Incorrect index test (not specific to point of care tests, and only compares sampling sites)
Fraser H, Gallacher D, Achana F, Court R, Taylor-Phillips S, Nduka C, et al. Rapid antigen detection and molecular tests for group A streptococcal infections for acute sore throat: systematic reviews and economic evaluation. Health technology assessment (Winchester, England). 2020;24(31):1-232.	Incorrect target condition (group A streptococcus)
Goncalves PF, Falcao LM, Pinheiro ID. Procalcitonin as biomarker of infection: Implications for evaluation and treatment. American Journal of Therapeutics. 2017;24(3):e243-e9.	No quality assessment of included studies, and searches of a single database only.
Guo R, Li J, Ma X, Pan L. The predictive value of neutrophil-to-lymphocyte ratio for chronic obstructive pulmonary disease: a systematic review and meta-analysis. Expert review of respiratory medicine. 2020;14(9):929-36.	No data on diagnostic accuracy outcomes.
Hankey B, Riley B. Towards evidence based emergency medicine: Best BETs from the manchester royal infirmary. Emergency Medicine Journal. 2015;32(6):493-5.	Not a systematic review

Hawkins NM, Khosla A, Virani SA, McMurray JJV, FitzGerald JM. B-type natriuretic peptides in chronic obstructive pulmonary disease: a systematic review. BMC pulmonary medicine. 2017;17(1):11.	No data on diagnostic accuracy outcomes.
He C, Wang B, Li D, Xu H, Shen Y. Performance of procalcitonin in diagnosing parapneumonic pleural effusions: A clinical study and meta-analysis. Medicine. 2017;96(33):e7829.	Incorrect target condition (parapneumonic pleural effusions)
Hobbs FD, Delaney BC, Fitzmaurice DA, Wilson S, Hyde CJ, Thorpe GH, et al. A review of near patient testing in primary care. Health technology assessment (Winchester, England). 1997;1(5):i-iv, 1-229.	Incorrect index tests.
Horita N, Miyazawa N, Kojima R, Kimura N, Inoue M, Ishigatsubo Y, et al. Sensitivity and specificity of the Streptococcus pneumoniae urinary antigen test for unconcentrated urine from adult patients with pneumonia: a meta-analysis. Respirology (Carlton, Vic). 2013;18(8):1177-83.	Incorrect target condition (pathogen specific tests for Streptococcus pneumoniae)
Huang C, Huang P-T, Yao J-Y, Li Z-W, Weng L-B, Guo X-G. Pooled analysis of nuclear acid sequence-based amplification for rapid diagnosis of Mycoplasma pneumoniae infection. Journal of clinical laboratory analysis. 2019;33(5):e22879.	Incorrect target condition (pathogen specific tests for Mycoplasma pneumoniae)
Huang Q, Xiong H, Shuai T, Wang Y, Zhang C, Zhang M, et al. The clinical value of suPAR in diagnosis and prediction for patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. Therapeutic advances in respiratory disease. 2020;14:1753466620938546.	Incorrect index test (not a point of care test)

Huang WJ, Huang GT, Zhan QM, Chen JL, Luo WT, Wu LH, et al. The neutrophil to lymphocyte ratio as a novel predictor of asthma and its exacerbation: a systematic review and meta-analysis. European review for medical and pharmacological sciences. 2020;24(22):11719-28.	No data on diagnostic accuracy outcomes.
Hughes JM, Penney C, Boyd S, Daley P. Risk of bias and limits of reporting in diagnostic accuracy studies for commercial point-of-care tests for respiratory pathogens. Epidemiology and Infection. 2018;146(6):747-56.	Searches were not comprehensive (single database only).
Iwase S, Nakada TA, Hattori N, Takahashi W, Takahashi N, Aizimu T, et al. Interleukin-6 as a diagnostic marker for infection in critically ill patients: A systematic review and meta-analysis. American Journal of Emergency Medicine. 2019;37(2):260-5.	Incorrect population (critically ill people).
Jacobus CH, Raja AS. How accurate are rapid influenza diagnostic tests? Annals of emergency medicine. 2013;61(1):89-90.	Not a systematic review
Jose BPdS, Camargos PAM, Cruz Filho AASd, Correa RdA. Diagnostic accuracy of respiratory diseases in primary health units. Revista da Associacao Medica Brasileira (1992). 2014;60(6):599-612.	No quality assessment of included studies, and searches of a single database only.
Joseph P, Godofsky E. Outpatient Antibiotic Stewardship: A Growing Frontier-Combining Myxovirus Resistance Protein A With Other Biomarkers to Improve Antibiotic Use. Open forum infectious diseases. 2018;5(2):ofy024.	No data on diagnostic accuracy outcomes.
Jullien S, Fitzgerald F, Keddie S, Baerenbold O, Bassat Q, Bradley J, et al. Diagnostic accuracy of multiplex respiratory pathogen panels for	Incorrect index test (not a point

influenza or respiratory syncytial virus infections: systematic review and meta-analysis. BMC infectious diseases. 2022;22(1):785.	of care multiplex test)
Kamat IS, Ramachandran V, Eswaran H, Guffey D, Musher DM. Procalcitonin to Distinguish Viral From Bacterial Pneumonia: A Systematic Review and Meta-analysis. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020;70(3):538-42.	Searches were not comprehensive (single database only).
Karakioulaki M, Stolz D. Biomarkers and clinical scoring systems in community-acquired pneumonia. Annals of Thoracic Medicine. 2019;14(3):165-72.	Not a systematic review
Kawasaki T, Nakagawa N, Murata M, Yasuo S, Yoshida T, Ando K, et al. Diagnostic accuracy of urinary antigen tests for legionellosis: A systematic review and meta-analysis. Respiratory investigation. 2022;60(2):205-14.	Incorrect target condition (Légionnaires disease)
Kazal LA. Re: Signs and symptoms that rule out community-acquired pneumonia in outpatient adults: A systematic review and meta-analysis. Journal of the American Board of Family Medicine. 2019;32(5):753.	Not a systematic review
Koo CY, Eisenhut M. Towards evidence-based emergency medicine: best BETs from the Manchester Royal Infirmary. Can inflammatory markers distinguish streptococcal from viral tonsillitis? Emergency medicine journal : EMJ. 2011;28(8):715-7.	Not a systematic review
Koski RR, Klepser ME. A systematic review of rapid diagnostic tests for influenza: considerations for the community pharmacist. Journal of the American Pharmacists Association : JAPhA. 2017;57(1):13-9.	No quality assessment of included studies.
Koutsokera A, Kostikas K, Nicod LP, Fitting J-W. Pulmonary biomarkers in COPD exacerbations: a systematic review. Respiratory research. 2013;14:111.	Incorrect index test (not point of care tests)

Krolicka AL, Kruczkowska A, Krajewska M, Kusztal MA. Hyponatremia in Infectious Diseases-A Literature Review. International journal of environmental research and public health. 2020;17(15).	No data on diagnostic accuracy outcomes.
Landry V, Coburn P, Kost K, Liu X, Li-Jessen NYK. Diagnostic Accuracy of Liquid Biomarkers in Airway Diseases: Toward Point-of-Care Applications. Frontiers in medicine. 2022;9:855250.	No quality assessment of included studies.
Lean WL, Arnup S, Danchin M, Steer AC. Rapid diagnostic tests for group A streptococcal pharyngitis: a meta-analysis. Pediatrics. 2014;134(4):771-81.	Incorrect target condition (group A streptococcus)
Li D, Shen Y, Qin J, Wan C, Zeng N, Chen L, et al. Diagnostic performance of C-reactive protein for parapneumonic pleural effusion: a meta-analysis. Annals of translational medicine. 2019;7(1):1.	Incorrect target condition (parapneumonic pleural effusions)
Li S, Huang X, Chen Z, Zhong H, Peng Q, Deng Y, et al. Neutrophil CD64 expression as a biomarker in the early diagnosis of bacterial infection: a meta-analysis. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2013;17(1):e12-23.	Incorrect population (children, inpatients and people with sepsis)
Lippi G, Meschi T, Cervellin G. Inflammatory biomarkers for the diagnosis, monitoring and follow-up of community-acquired pneumonia: clinical evidence and perspectives. European journal of internal medicine. 2011;22(5):460-5.	Not a systematic review
Long B, Long D, Koyfman A. Emergency Medicine Evaluation of Community-Acquired Pneumonia: History, Examination, Imaging and	No quality assessment of

Laboratory Assessment, and Risk Scores. Journal of Emergency Medicine. 2017;53(5):642-52.	included studies.
Mahony JB. Detection of respiratory viruses by molecular methods. Clinical Microbiology Reviews. 2008;21(4):716-47.	Not a systematic review
Malinovska A, Hernried B, Lin A, Badaki-Makun O, Fenstermacher K, Ervin AM, et al. Monocyte Distribution Width as a Diagnostic Marker for Infection: A Systematic Review and Meta-Analysis. Chest. 2023.	Incorrect index test (not a point of care test)
Marchello CS, Ebell MH. Response: Re: Signs and symptoms that rule out community-acquired pneumonia in outpatient adults: A systematic review and meta-analysis. Journal of the American Board of Family Medicine. 2019;32(5):753-4.	Letter to the Editor, no primary data.
Marchello CS, Ebell MH, Dale AP, Harvill ET, Shen Y, Whalen CC. Signs and Symptoms That Rule out Community-Acquired Pneumonia in Outpatient Adults: A Systematic Review and Meta-Analysis. Journal of the American Board of Family Medicine : JABFM. 2019;32(2):234-47.	Searches were not comprehensive (single database only).
Masot O, Cox A, Mold F, Sund-Levander M, Tingstrom P, Boersema GC, et al. Decision support-tools for early detection of infection in older people (aged> 65 years): a scoping review. BMC geriatrics. 2022;22(1):552.	No data on diagnostic accuracy outcomes.
McCrory DC, Brown C, Gelfand SE, Bach PB. Management of acute exacerbations of COPD: a summary and appraisal of published evidence. Chest. 2001;119(4):1190-209.	Not a systematic review
McMullen AR, Anderson NW, Burnhamfor CAD. Pathology consultation on influenza diagnostics. American Journal of Clinical Pathology. 2016;145(4):440-8.	Not a systematic review

Mehdipour A, Wiley E, Richardson J, Beauchamp M, Kuspinar A. The Performance of Digital Monitoring Devices for Oxygen Saturation and Respiratory Rate in COPD: A Systematic Review. COPD. 2021;18(4):469-75.	No data on diagnostic accuracy outcomes.
Memar MY, Baghi HB. Presepsin: A promising biomarker for the detection of bacterial infections. Biomedicine and Pharmacotherapy. 2019;111:649-56.	Not a systematic review
Metlay JP, Kapoor WN, Fine MJ. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA. 1997;278(17):1440-5.	Searches were not comprehensive (single database only).
Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and treatment of adults with community-acquired pneumonia. American Journal of Respiratory and Critical Care Medicine. 2019;200(7):E45-E67.	Not a systematic review
Milas GP, Issaris V, Papavasileiou V. Blood urea nitrogen to albumin ratio as a predictive factor for pneumonia: A meta-analysis. Respiratory medicine and research. 2022;81:100886.	No data on diagnostic accuracy outcomes.
Mohan A, Harikrishna J. Biomarkers for the diagnosis of bacterial infections: In pursuit of the 'Holy Grail'. Indian Journal of Medical Research. 2015;141(3):271-3.	Not a systematic review
Muller B, Christ-Crain M, Schuetz P. Meta-analysis of procalcitonin for sepsis detection. Lancet Infectious Diseases. 2007;7(8):498-9.	Not a systematic review
Ni W, Bao J, Yang D, Xi W, Wang K, Xu Y, et al. Potential of serum procalcitonin in predicting bacterial exacerbation and guiding antibiotic administration in severe COPD exacerbations: a systematic review and	Incorrect population (all participants

meta-analysis. Infectious diseases (London, England). 2019;51(9):639-50.	were hospitalised)
Ojha SC, Chen K, Sun C, Ahmed S, Sheng Y-J, Deng C-L. Clinical Relevance of Xpert MRSA/SA in Guiding Therapeutic Decisions for Staphylococcal Infections: A Diagnostic Test Accuracy Analysis. Infectious diseases and therapy. 2022;11(3):1205-27.	Incorrect target condition (not assessing acute respiratory infections)
Onyenekwu CP, Okwundu CI, Ochodo EA. Procalcitonin, C-reactive protein, and presepsin for the diagnosis of sepsis in adults and children. Cochrane Database of Systematic Reviews. 2017;2017(4):CD012627.	Protocol, not a systematic review
Otten T, de Mast Q, Koeneman B, Althaus T, Lubell Y, van der Ven A. Value of C-reactive protein in differentiating viral from bacterial aetiologies in patients with non-malaria acute undifferentiated fever in tropical areas: a meta-analysis and individual patient data study. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2021;115(10):1130-43.	Incorrect population (people with fever, not ARI)
Pearson M. Chronic Obstructive Pulmonary Disease: National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. Thorax. 2004;59:1-232.	Not a systematic review
Relich RF, Abbott AN. Syndromic and Point-of-Care Molecular Testing. Clinics in Laboratory Medicine. 2022;42(4):507-31.	Not a systematic review
Renier W, Winckelmann KH-v, Verbakel JY, Aertgeerts B, Buntinx F. Signs and symptoms in adult patients with acute dyspnea: a systematic review and meta-analysis. European journal of emergency medicine : official journal of the European Society for Emergency Medicine. 2018;25(1):3-11.	Incorrect population (not people with suspected ARI)

Richards S, Conover C, DiOrio M, Park S, Balish A, Garten R, et al. Evaluation of rapid influenza diagnostic tests for influenza A (H3N2)v virus and updated case count - United States, 2012. Morbidity and Mortality Weekly Report. 2012;61(32):619-21.	Not a systematic review
Said MA, Johnson HL, Nonyane BAS, Deloria-Knoll M, O'Brien KL, Andreo F, et al. Estimating the burden of pneumococcal pneumonia among adults: a systematic review and meta-analysis of diagnostic techniques. PloS one. 2013;8(4):e60273.	No data on diagnostic accuracy outcomes.
Salez N, Nougairede A, Ninove L, Zandotti C, De Lamballerie X, Charrel RN. Xpert Flu for point-of-care diagnosis of human influenza in industrialized countries. Expert Review of Molecular Diagnostics. 2014;14(4):411-8.	Not a systematic review
Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. BMC medicine. 2011;9:107.	Not a systematic review
Sheng F, Chen L, Lin H, Wu H. Systematic review and meta-analysis: value of venous blood gas in the diagnosis of acute exacerbation of chronic obstructive pulmonary disease in Emergency Department. Annals of palliative medicine. 2022;11(4):1473-81.	No data on diagnostic accuracy outcomes.
Shimada T, Noguchi Y, Jackson JL, Miyashita J, Hayashino Y, Kamiya T, et al. Systematic review and metaanalysis: urinary antigen tests for Legionellosis. Chest. 2009;136(6):1576-85.	Incorrect target condition (Légionnaires disease)
Sierra R. C-reactive protein and procalcitonin as markers of infection, inflammatory response, and sepsis. Clinical Pulmonary Medicine. 2007;14(3):127-39.	Not a systematic review
Sinclair A, Xie X, Teltscher M, Dendukuri N. Systematic review and meta-analysis of a urine-based pneumococcal antigen test for diagnosis	Incorrect target condition (pathogen specific tests for

of community-acquired pneumonia caused by Streptococcus pneumoniae. Journal of clinical microbiology. 2013;51(7):2303-10.	Streptococcus pneumoniae)
Smith MN, Brotherton AL, Lusardi K, Tan CA, Hammond DA. Systematic Review of the Clinical Utility of Methicillin-Resistant Staphylococcus aureus (MRSA) Nasal Screening for MRSA Pneumonia. The Annals of pharmacotherapy. 2019;53(6):627-38.	Incorrect population (inpatients/ICU)
Stewart EH, Davis B, Clemans-Taylor BL, Littenberg B, Estrada CA, Centor RM. Rapid antigen group A streptococcus test to diagnose pharyngitis: a systematic review and meta-analysis. PloS one. 2014;9(11):e111727.	Incorrect target condition (group A streptococcus)
Stokes K, Castaldo R, Federici C, Pagliara S, Maccaro A, Cappuccio F et al. The use of artificial intelligence systems in diagnosis of pneumonia via signs and symptoms: A systematic review. Biomedical Signal Processing and Control. 2022; 72:103325	No quality assessment of included studies (use of the STARD reporting checklist, not a methodological assessment).
Su X, Lei T, Yu H, Zhang L, Feng Z, Shuai T, et al. NT-proBNP in Different Patient Groups of COPD: A Systematic Review and Meta-Analysis. International journal of chronic obstructive pulmonary disease. 2023;18:811-25.	No data on diagnostic accuracy outcomes.
Subsoontorn P, Lohitnavy M, Kongkaew C. The diagnostic accuracy of isothermal nucleic acid point-of-care tests for human coronaviruses: A systematic review and meta-analysis. Scientific reports. 2020;10(1):22349.	Incorrect index test (predominantly COVID-19)

Tang J-H, Gao D-P, Zou P-F. Comparison of serum PCT and CRP levels in patients infected by different pathogenic microorganisms: a systematic review and meta-analysis. Brazilian journal of medical and biological research = Revista brasileira de pesquisas medicas e biologicas. 2018;51(7):e6783.	No data on diagnostic accuracy outcomes.
Tenover FC. The role for rapid molecular diagnostic tests for infectious diseases in precision medicine. Expert Review of Precision Medicine and Drug Development. 2018;3(1):69-77.	Not a systematic review
Thai TN, Dale AP, Ebell MH. Signs and symptoms of Group A versus Non-Group A strep throat: A meta-analysis. Family practice. 2018;35(3):231-8.	Searches were not comprehensive (single database only).
Thornton HV, Turner KME, Harrison S, Hammond A, Hawcroft C, Hay AD. Assessing the potential of upper respiratory tract point-of-care testing: a systematic review of the prognostic significance of upper respiratory tract microbes. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2019;25(11):1339-46.	No data on diagnostic accuracy outcomes.
Ticinesi A, Scarlata S, Nouvenne A, Lauretani F, Incalzi RA, Ungar A. The Geriatric Patient: The Ideal One for Chest Ultrasonography? A Review From the Chest Ultrasound in the Elderly Study Group (GRETA) of the Italian Society of Gerontology and Geriatrics (SIGG). Journal of the American Medical Directors Association. 2020;21(4):447-54.e6.	Incorrect index test (chest ultrasound)
Vachhani R, Patel T, Centor RM, Estrada CA. Sensitivity for Diagnosing Group A Streptococcal Pharyngitis from Manufacturers is 10% Higher than Reported in Peer-Reviewed Publications. Southern medical journal. 2017;110(1):59-64.	Incorrect target condition (group A streptococcus)

van de Kant KDG, van der Sande LJTM, Jobsis Q, van Schayck OCP, Dompeling E. Clinical use of exhaled volatile organic compounds in pulmonary diseases: a systematic review. Respiratory research. 2012;13:117.	Incorrect population (not people with ARI)
van de Pol AC, van der Zalm MM, Jansen NJG, van der Ent CK, van Loon AM, Kimpen JLL, et al. Conventional vs molecular viral tests for respiratory viruses: A systematic review. Current Respiratory Medicine Reviews. 2010;6(4):300-9.	Incorrect population (children)
Wang H, Li F, Huang H, Wu F, Chen L, Zhang D, et al. Serum surfactant protein D is a potential biomarker for chronic obstructive pulmonary disease: A Systematic Review and Meta-analysis. Clinical Laboratory. 2019;65(12):2387-95.	No data on diagnostic accuracy outcomes.
Willis BH, Coomar D, Baragilly M. Comparison of Centor and McIsaac scores in primary care: a meta-analysis over multiple thresholds. The British journal of general practice : the journal of the Royal College of General Practitioners. 2020;70(693):e245-e54.	Incorrect target condition (group A streptococcus)
Wroblewski T, Marcisz C. Procalcitonin as a biomarker of acute lower respiratory tract infections. Expert Opinion on Medical Diagnostics. 2009;3(1):67-79.	Not a systematic review
Xie L-M, Yin X, Xie T-A, Su J-W, Huang Q, Zhang J-H, et al. Meta-Analysis of the Diagnostic Efficacy of the Luminex xTAG Respiratory Viral Panel FAST v2 Assay for Respiratory Viral Infections. Yonsei medical journal. 2022;63(1):95-103.	Incorrect index test (not a point of care multiplex test)
Xie X, Sinclair A, Dendukuri N. Evaluating the accuracy and economic value of a new test in the absence of a perfect reference test. Research synthesis methods. 2017;8(3):321-32.	Not a systematic review
Yancey JR, Nelson MD, Whalen NJ. Procalcitonin for Diagnosis, Risk Assessment, and Prognosis of Respiratory Tract Infections. American Family Physician. 2022;106(3):333-4.	Not a systematic review

Yasuo S, Murata M, Nakagawa N, Kawasaki T, Yoshida T, Ando K, et al. Diagnostic accuracy of urinary antigen tests for pneumococcal pneumonia among patients with acute respiratory failure suspected pneumonia: a systematic review and meta-analysis. BMJ open. 2022;12(8):e057216.	Incorrect target condition (pathogen specific tests for Streptococcus pneumoniae)
Ye W, Huang Q-D, Tang T-Y, Qin G-Y. Diagnostic value of pentraxin 3 in respiratory tract infections: A meta-analysis. Medicine. 2020;99(14):e19532.	Incorrect population (people with ventilator-associated pneumonia)
Yoon SH, Min IK, Ahn JG. Immunochromatography for the diagnosis of Mycoplasma pneumoniae infection: A systematic review and meta-analysis. PloS one. 2020;15(3):e0230338.	Incorrect target condition (pathogen specific tests for Mycoplasma pneumoniae)
Yousefi A, Farsiani H, Ghazvini K, Yousefi M. Multiplex pcr systems for the isolation of respiratory bacterial infection: Systematic review. International Journal of Pharmaceutical Research. 2021;13(1):6189-204.	Incorrect population (children) and not point of care tests.

Excluded primary studies for white blood cell count

Ahn JM, Hwang SO, Moon JS, Lee SJ, Cha YS. Predictive Value of the Neutrophil-to-Lymphocyte Ratio for the Diagnosis of Pneumonia in Normothermic Dyspneic Patients with Chronic Heart Failure in the Emergency Department. Journal of Emergency Medicine. 2020;58(6):892-901.	Wrong population

Aronen M, Viikari L, Kohonen I, Vuorinen T, Hameenaho M, Wuorela M, et al. Respiratory tract virus infections in the elderly with pneumonia. BMC geriatrics. 2019;19(1):111.	Wrong population
Ashkenazi-Hoffnung L, Oved K, Navon R, Friedman T, Boico O, Paz M, et al. A host-protein signature is superior to other biomarkers for differentiating between bacterial and viral disease in patients with respiratory infection and fever without source: a prospective observational study. European Journal of Clinical Microbiology and Infectious Diseases. 2018;37(7):1361-71.	Wrong population
Ates H, Ates I, Bozkurt B, Celik HT, Ozol D, Yildirim Z. What is the most reliable marker in the differential diagnosis of pulmonary embolism and community-acquired pneumonia? Blood Coagulation and Fibrinolysis. 2016;27(3):252-8.	Wrong study design
Ayala-Lopez N, Peaper DR, Harb R. Procalcitonin Correlates With but Is Not Superior to Other Diagnostic Markers of Bacterial Pneumonia. American journal of clinical pathology. 2020.	No 2x2 data reported
Bello S, Minchole E, Fandos S, Lasierra AB, Ruiz MA, Simon AL, et al. Inflammatory response in mixed viral-bacterial community-acquired pneumonia. BMC Pulmonary Medicine. 2014;14(1):123.	No 2x2 data reported
Berhane M, Melku M, Amsalu A, Enawgaw B, Getaneh Z, Asrie F. The role of neutrophil to lymphocyte count ratio in the differential diagnosis of pulmonary tuberculosis and bacterial community-acquired pneumonia: A cross-sectional study at Ayder and Mekelle Hospitals, Ethiopia. Clinical Laboratory. 2019;65(4):527-33.	Wrong study design
Bochud PY, Moser F, Erard P, Verdon F, Studer JP, Villard G, et al. Community-acquired pneumonia: A prospective outpatient study. Medicine. 2001;80(2):75-87.	No 2x2 data reported
Cai R, Li H, Tao Z. Heparin-binding protein and procalcitonin in the diagnosis of pathogens causing community-acquired pneumonia in adult patients: A retrospective study. PeerJ. 2021;9:11056.	Wrong population

Chang CH, Tsao KC, Hu HC, Huang CC, Kao KC, Chen NH, et al. Procalcitonin and C-reactive protein cannot differentiate bacterial or viral infection in COPD exacerbation requiring emergency department visits. International Journal of COPD. 2015;10:767-74.	No 2x2 data reported
Choi J, Oh JY, Lee YS, Hur GY, Lee SY, Shim JJ, et al. The association between blood eosinophil percent and bacterial infection in acute exacerbation of chronic obstructive pulmonary disease. International Journal of COPD. 2019;14:953-9.	No 2x2 data reported
Cox AJ, Gleeson M, Pyne DB, Callister R, Hopkins WG, Fricker PA. Clinical and laboratory evaluation of upper respiratory symptoms in elite athletes. Clinical Journal of Sport Medicine. 2008;18(5):438-45.	No 2x2 data reported
Dal Negro RW, Micheletto C, Tognella S, Visconti M, Guerriero M, Sandri MF. A two-stage logistic model based on the measurement of pro-inflammatory cytokines in bronchial secretions for assessing bacterial, viral, and non-infectious origin of COPD exacerbations. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2005;2(1):7-16.	No 2x2 data reported
Dixon G, Lama-Lopez A, Bintcliffe OJ, Morley AJ, Hooper CE, Maskell NA. The role of serum procalcitonin in establishing the diagnosis and prognosis of pleural infection. Respiratory Research. 2017;18(1):30.	Frozen samples used
Dowell SF, Anderson LJ, Gary Jr HE, Erdman DD, Plouffe JF, File Jr TM, et al. Respiratory syncytial virus is an important cause of community-acquired lower respiratory infection among hospitalized adults. Journal of Infectious Diseases. 1996;174(3):456-62.	Wrong population
El-Azeem AA, Hamdy G, Saraya M, Fawzy E, Anwar E, Abdulattif S. The role of procalcitonin as a guide for the diagnosis, prognosis, and decision of antibiotic therapy for lower respiratory tract infections. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(4):687-95.	No 2x2 data reported
Fernando Saldias P, Orlando Diaz P, Jorge Dreyse D, Aldo Gaggero B, Christian Sandoval A, Carmen Lisboa B. Etiology and biomarkers of	Not in English

systemic inflammation in mild to moderate COPD exacerbations. Revista Medica de Chile. 2012;140(1):10-8.	
Fredman G, Kolpen M, Hertz FB, Petersen PT, Jensen AV, Baunbaek-Egelund G, et al. The inflamed sputum in lower respiratory tract infection: l-lactate levels are correlated to neutrophil accumulation. APMIS. 2019;127(2):72-9.	No 2x2 data reported
Gao S, Duan Y, Chen J, Wang J. Evaluation of Blood Markers at Admission for Predicting Community Acquired Pneumonia in Chronic Obstructive Pulmonary Disease. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2021;18(5):557-66.	Wrong population
Han Q, Wen X, Wang L, Han X, Shen Y, Cao J, et al. Role of hematological parameters in the diagnosis of influenza virus infection in patients with respiratory tract infection symptoms. Journal of clinical laboratory analysis. 2020:e23191.	Wrong population
Holmberg H, Bodin L, Jonsson I, Krook A. Rapid aetiological diagnosis of pneumonia based on routine laboratory features. Scandinavian Journal of Infectious Diseases. 1990;22(5):537-45.	Wrong population
Kerttula Y, Leinonen M, Koskela M, Makela PH. The aetiology of pneumonia. Application of bacterial serology and basic laboratory methods. Journal of Infection. 1987;14(1):21-30.	Wrong population
Kragsbjerg P, Jones I, Vikerfors T, Holmberg H. Diagnostic value of blood cytokine concentrations in acute pneumonia. Thorax. 1995;50(12):1253-7.	Wrong population
Lagerstrom F, Engfeldt P, Holmberg H. C-reactive protein in diagnosis of community-acquired pneumonia in adult patients in primary care. Scandinavian Journal of Infectious Diseases. 2006;38(11):964-9.	No 2x2 data reported
Lee JY, Hwang SJ, Shim JW, Jung HL, Park MS, Woo HY, et al. Clinical significance of serum procalcitonin in patients with community-acquired lobar pneumonia. The Korean journal of laboratory medicine. 2010;30(4):406-13.	Wrong population

Lee TC, Taggart LR, Mater B, Katz K, McGeer A. Predictors of pandemic influenza infection in adults presenting to two urban emergency departments, Toronto, 2009. Canadian Journal of Emergency Medicine. 2011;13(1):7-12.	Wrong study design
Lehtomaki K, Leinonen M, Takala A, Hovi T, Herva E, Koskela M. Etiological diagnosis of pneumonia in military conscripts by combined use of bacterial culture and serological methods. European Journal of Clinical Microbiology and Infectious Diseases. 1988;7(3):348-54.	Wrong study design
Li Y, Van Houten CB, Boers SA, Jansen R, Cohen A, Engelhard D, et al. The diagnostic value of nasal microbiota and clinical parameters in a multi-parametric prediction model to differentiate bacterial versus viral infections in lower respiratory tract infections. PLoS ONE. 2022;17(4):e0267140.	Wrong population
Marcos MA, Camps M, Pumarola T, Martinez JA, Martinez E, Mensa J, et al. The role of viruses in the aetiology of community-acquired pneumonia in adults. Antiviral Therapy. 2006;11(3):351-9.	No 2x2 data reported
Mirete Ferrer JC, Gutierrez Rodero F, Hernandez Aguado I, del Mar Masia Canuto M, Rodriguez Diaz JC, Royo Garia G. Community-acquired pneumonia associated with influenza virus. Medicina Clinica. 2002;118(16):622-6.	Not in English
Noweta K, Frankowska M, Grzelewska-Rzymowska I. Exacerbations of chronic obstructive pulmonary disease and the role of sputum bacteriological examination. Pneumonologia i Alergologia Polska. 2006;74(4):396-402.	Not in English
Patel B, Oye M, Norez D, Isache C. Peripheral blood lymphocyte-to-monocyte ratio as a screening marker for influenza infection. Journal of Investigative Medicine. 2021;69(1):47-51.	Wrong target condition
Pauksen K, Elfman L, Ulfgren AK, Venge P. Serum levels of granulocyte-colony stimulating factor (G-CSF) in bacterial and viral infections, and in atypical pneumonia. British Journal of Haematology. 1994;88(2):256-60.	Wrong study design

Ponka A, Sarna S. Differential diagnosis of viral, mycoplasmal and bacteraemic pneumococcal pneumonias on admission to hospital. European Journal of Respiratory Diseases. 1983;64(5):360-8.	Wrong study design
Ruiz-Gonzalez A, Falguera M, Vives M, Nogues A, Porcel JM, Rubio-Caballero M. Community-acquired pneumonia: Development of a bedside predictive model and scoring system to identify the aetiology. Respiratory Medicine. 2000;94(5):505-10.	Wrong population
Ruiz-Gonzalez A, Saez-Huerta E, Martinez-Alonso M, Bernet-Sanchez A, Porcel JM. A Simple Scoring System to Differentiate Bacterial from Viral Infections in Acute Exacerbations of COPD Requiring Hospitalization. International Journal of COPD. 2022;17:773-9.	No 2x2 data reported
Sambursky R, Shapiro N. Evaluation of a combined MxA and CRP point-of-care immunoassay to identify viral and/or bacterial immune response in patients with acute febrile respiratory infection. European clinical respiratory journal. 2015;2:28245.	No 2x2 data reported
Sim JK, Oh JY, Lee EJ, Hur GY, Lee SH, Lee SY, et al. Serum procalcitonin for differential diagnosis of acute exacerbation and bacterial pneumonia in patients with interstitial lung disease. American Journal of the Medical Sciences. 2016;351(5):499-505.	No 2x2 data reported
Sirohi P, Barodia MK, Nehara HR, Chhimpa AR, Dabas A, Kumar R. Application of haematological indices in the diagnosis of swine influenza infection in adults. Journal of Clinical and Diagnostic Research. 2020;14(9):OC32-OC5.	Wrong population
Stein M, Lipman-Arens S, Oved K, Cohen A, Bamberger E, Navon R, et al. A novel host-protein assay outperforms routine parameters for distinguishing between bacterial and viral lower respiratory tract infections. Diagnostic Microbiology and Infectious Disease. 2018;90(3):206-13.	Wrong population
Tanriverdi H, Ornek T, Erboy F, Altinsoy B, Uygur F, Atalay F, et al. Comparison of diagnostic values of procalcitonin, C-reactive protein and blood neutrophil/lymphocyte ratio levels in predicting bacterial infection in	Wrong population

hospitalized patients with acute exacerbations of COPD. Wiener Klinische Wochenschrift. 2015;127(19):756-63.	
Titova E, Aune MW, Fonn K, Henriksen AH, Asberg A. Neutrophil CD64 Expression as a Diagnostic Marker in Patients Hospitalized with Exacerbations of COPD: A Prospective Observational Study. Lung. 2015;193(5):717-24.	Wrong population
van de Geijn GJM, Denker S, Meuleman-van Waning V, Koeleman HGM, Birnie E, Braunstahl GJ, et al. Evaluation of new laboratory tests to discriminate bacterial from nonbacterial chronic obstructive pulmonary disease exacerbations. International Journal of Laboratory Hematology. 2016;38(6):616-28.	Wrong study design
Yoon NB, Son C, Um SJ. Role of the neutrophil-lymphocyte count ratio in the differential diagnosis between pulmonary tuberculosis and bacterial community-acquired pneumonia. Annals of Laboratory Medicine. 2013;33(2):105-10.	Wrong study design

Excluded primary studies for multiplex tests

Akashi Y, Suzuki H, Ueda A, Hirose Y, Hayashi D, Imai H, et al. Analytical and clinical evaluation of a point-of-care molecular diagnostic system and its influenza A/B assay for rapid molecular detection of the influenza virus. Journal of Infection and Chemotherapy. 2019;25(8):578-83.	Wrong population
Alby K, Popowitch EB, Miller MB. Comparative evaluation of the nanosphere verigene RV+ assay and the simplexa flu A/B & RSV kit for detection of influenza and respiratory syncytial viruses. Journal of Clinical Microbiology. 2013;51(1):352-3.	Frozen samples used

Arbefeville S, Thonen-Kerr E, Ferrieri P. Prospective and Retrospective Evaluation of the Performance of the FDA-Approved Cepheid Xpert Flu/RSV XC Assay. Lab Medicine. 2017;48(4):E53-E6.	Frozen samples used
Babady NE, England MR, Smith KLJ, He T, Wijetunge DS, Tang YW, et al. Multicenter evaluation of the eplex respiratory pathogen panel for the detection of viral and bacterial respiratory tract pathogens in nasopharyngeal swabs. Journal of Clinical Microbiology. 2018;56(2):e01658-17.	Wrong population
Balada-Llasat JM, LaRue H, Kelly C, Rigali L, Pancholi P. Evaluation of commercial ResPlex II v2.0, MultiCode-PLx, and xTAG respiratory viral panels for the diagnosis of respiratory viral infections in adults. Journal of Clinical Virology. 2011;50(1):42-5.	Not point of care
Banerjee D, Kanwar N, Hassan F, Lankachandra K, Selvarangan R. Comparative analysis of Four sample-to-answer influenza A/B and RSV nucleic acid amplification assays using adult respiratory specimens. Journal of Clinical Virology. 2019;118:9-13.	Frozen samples used
Bayart JL, Gillot C, Dogne JM, Roussel G, Verbelen V, Favresse J, et al. Clinical performance evaluation of the Fluorecare SARS-CoV-2 & Influenza A/B & RSV rapid antigen combo test in symptomatic individuals. Journal of Clinical Virology. 2023;161:105419.	Frozen samples used
Bennett S, MacLean A, Gunson R. Verification of Cepheid Xpert Xpress Flu/RSV assay for use with gargle samples, sputa and endotracheal secretions. The Journal of hospital infection. 2019;101(1):114-5.	No 2x2 data reported
Binnicker MJ, Espy MJ, Irish CL, Vetter EA. Direct detection of influenza A and B viruses in less than 20 minutes using a commercially available rapid PCR Assay. Journal of Clinical Microbiology. 2015;53(7):2353-4.	Frozen samples used
Blank C. New respiratory assay panel provides quick results for several flu strains. Drug Topics. 2011;155(11).	Wrong publication type

Boerger AC, Binnicker MJ. Comparison of the Panther Fusion respiratory panels to routine methods for detection of viruses in upper and lower respiratory tract specimens. Diagnostic microbiology and infectious disease. 2020;97(2):115014.	Frozen samples used
Boers SA, Melchers WJG, Peters CJA, Toonen M, McHugh MP, Templeton KE, et al. Multicenter evaluation of QIAstat-Dx respiratory panel V2 for detection of viral and bacterial respiratory pathogens. Journal of Clinical Microbiology. 2020;58(6):e01793-19.	Unclear population and/or setting
Boukli N, Flamand C, Chea KL, Heng L, Keo S, Sour K, et al. One assay to test them all: Multiplex assays for expansion of respiratory virus surveillance. Frontiers in Medicine. 2023;10:1161268.	Unclear population and/or setting
Butt SA, Maceira VP, McCallen ME, Stellrecht KA. Comparison of three commercial RT-PCR systems for the detection of respiratory viruses. Journal of Clinical Virology. 2014;61(3):406-10.	Wrong population
Chan M, Koo SH, Jiang B, Lim PQ, Tan TY. Comparison of the Biofire FilmArray Respiratory Panel, Seegene AnyplexII RV16, and Argene for the detection of respiratory viruses. Journal of Clinical Virology. 2018;106:13-7.	No 2x2 data reported
Chen JH, Lam HY, Yip CC, Cheng VC, Chan JF, Leung TH, et al. Evaluation of the molecular Xpert Xpress Flu/RSV assay vs. Alere i Influenza A & B assay for rapid detection of influenza viruses. Diagnostic Microbiology and Infectious Disease. 2018;90(3):177-80.	Wrong population
Chen JHK, Lam HY, Yip CCY, Wong SCY, Chan JFW, Edmond SK, et al. Clinical evaluation of the new high-throughput luminex nxtag respiratory pathogen panel assay for multiplex respiratory pathogen detection. Journal of Clinical Microbiology. 2016;54(7):1820-5.	Unclear population and/or setting
Chen L, Tian Y, Chen S, Liesenfeld O. Performance of the Cobas(R) Influenza A/B Assay for Rapid Pcr-Based Detection of Influenza Compared to	Unclear population

Prodesse ProFlu+ and Viral Culture. European journal of microbiology & immunology. 2015;5(4):236-45.	and/or setting
Cheng A, Riedel S, Arnaout R, Kirby JE. Verification of the Abbott Alinity m Resp-4-Plex assay for detection of SARS-CoV-2, influenza A/B, and respiratory syncytial virus. Diagnostic Microbiology and Infectious Disease. 2022;102(2):115575.	Frozen samples used
Cho HJ, Jang JW, Ko SY, Choi SH, Lim CS, An SSA. Evaluation and verification of the nanosphere Verigene RV+ assay for detection of influenza A/B and H1/H3 subtyping. Journal of Medical Virology. 2015;87(1):18-24.	Frozen samples used
Cohen DM, Kline J, May LS, Harnett GE, Gibson J, Liang SY, et al. Accurate pcr detection of influenza a/b and respiratory syncytial viruses by use of cepheid xpert flu+rsv xpress assay in point-of-care settings: Comparison to prodesse proflu+. Journal of Clinical Microbiology. 2018;56(2):e01237-17.	Unclear population and/or setting
DiMaio MA, Sahoo MK, Waggoner J, Pinsky BA. Comparison of Xpert Flu rapid nucleic acid testing with rapid antigen testing for the diagnosis of influenza A and B. Journal of Virological Methods. 2012;186(1):137-40.	Frozen samples used
Doern CD, Lacey D, Huang R, Haag C. Evaluation and implementation of FilmArray Version 1.7 for improved detection of adenovirus respiratory tract infection. Journal of Clinical Microbiology. 2013;51(12):4036-9.	Wrong population
Domnich A, Bruzzone B, Trombetta CS, De Pace V, Ricucci V, Varesano S, et al. Rapid differential diagnosis of SARS-CoV-2, influenza A/B and respiratory syncytial viruses: Validation of a novel RT-PCR assay. Journal of Clinical Virology. 2023;161:105402.	Frozen samples used
Dugas AF, Valsamakis A, Gaydos CA, Forman M, Hardick J, Kidambi P, et al. Evaluation of the Xpert Flu Rapid PCR assay in high-risk emergency department patients. Journal of Clinical Microbiology. 2014;52(12):4353-5.	Frozen samples used

Edin A, Eilers H, Allard A. Evaluation of the Biofire Filmarray Pneumonia panel plus for lower respiratory tract infections. Infectious Diseases. 2020;52(7):479-88.	Wrong population
Ellis J, Guest P, Lawson V, Loecherbach J, Lindner N, McCulloch A. Performance Evaluation of the Microfluidic Antigen LumiraDx SARS-CoV-2 and Flu A/B Test in Diagnosing COVID-19 and Influenza in Patients with Respiratory Symptoms. Infectious Diseases and Therapy. 2022;11(6):2099-2109.	Frozen samples used
Folgueira L, Moral N, Pascual C, Delgado R. Comparison of the Panther Fusion and Allplex assays for the detection of respiratory viruses in clinical samples. PLoS ONE. 2019;14(12):e0226403.	Wrong population
Galar A, Catalan P, Vesperinas L, Miguens I, Munoz L, Garcia-Espona A, et al. Use of Saliva Swab for Detection of Influenza Virus in Patients Admitted to an Emergency Department. Microbiology Spectrum. 2021;9(1):1-6.	Wrong population
Ganzenmueller T, Kaiser R, Baier C, Wehrhane M, Hilfrich B, Witthuhn J, et al. Comparison of the performance of the Panther Fusion respiratory virus panel to R-Gene and laboratory developed tests for diagnostic and hygiene screening specimens from the upper and lower respiratory tract. Journal of medical microbiology. 2020;69(3):427-35.	Wrong population
Gast KB, Vrolijk ACIM, Bergmans AMC, Geelen TH, Kluytmans JAJW, Pas SD. Clinical performance of the Xpert Xpress Flu/RSV assay for the detection of influenza A, B, and respiratory syncytial virus on ESwabTM medium. Journal of Clinical Virology Plus. 2022;2(1):100066.	Wrong population
Gibson J, Schechter-Perkins EM, Mitchell P, Mace S, Tian Y, Williams K, et al. Multi-center evaluation of the cobas Liat Influenza A/B & RSV assay for rapid point of care diagnosis. Journal of Clinical Virology. 2017;95:5-9.	Unclear population and/or setting

Goldenberg SD, Edgeworth JD. The Enigma ML FluAB-RSV assay: A fully automated molecular test for the rapid detection of influenza A, B and respiratory syncytial viruses in respiratory specimens. Expert Review of Molecular Diagnostics. 2015;15(1):23-32.	Wrong study design
Gomez S, Prieto C, Vera C, Otero JR, Folgueira L. Evaluation of a new rapid diagnostic test for the detection of influenza and RSV. Enfermedades Infecciosas y Microbiologia Clinica. 2016;34(5):298-302.	Unable to retrieve
Gosert R, Naegele K, Hirsch HH. Comparing the Cobas Liat Influenza A/B and respiratory syncytial virus assay with multiplex nucleic acid testing. Journal of Medical Virology. 2019;91(4):582-7.	Wrong population
Haglund S, Quttineh M, Nilsson Bowers A, Matussek A, Henningsson AJ. Xpert Flu as a rapid diagnostic test for respiratory tract viral infection: evaluation and implementation as a 24/7 service. Infectious Diseases. 2018;50(2):140-4.	Unclear population and/or setting
Haigh J, Cutino-Moguel MT, Wilks M, Welch CA, Melzer M. A service evaluation of simultaneous near-patient testing for influenza, respiratory syncytial virus, Clostridium difficile and norovirus in a UK district general hospital. Journal of Hospital Infection. 2019;103(4):441-6.	Unclear population and/or setting
Hindiyeh M, Kolet L, Meningher T, Weil M, Mendelson E, Mandelboim M. Evaluation of Simplexa flu A/B & RSV for direct detection of influenza viruses (A and B) and respiratory syncytial virus in patient clinical samples. Journal of Clinical Microbiology. 2013;51(7):2421-4.	Frozen samples used
Ho YII, Wong AH, Lai RWM. Comparison of the Cepheid Xpert Xpress Flu/RSV Assay to inhouse Flu/RSV triplex real-time RT-PCR for rapid molecular detection of Influenza A, Influenza B and Respiratory Syncytial Virus in respiratory specimens. Journal of Medical Microbiology. 2018;67(11):1576-80.	Unclear population and/or setting
Hughes AEO, Webber DM, Wallace MA, Johnson C, Burnham CA, Anderson NW. Comparable Detection of Viral Pathogens in Lower Respiratory Tract	Wrong population

Specimens With the BioFire Respiratory Panel 2 and BioFire Pneumonia Panel. Journal of clinical microbiology. 2020.	
Hur KH, Sung H, Kim MN. Comparative evaluation of two automated multiplex RT-PCR tests for rapid detection of influenza and respiratory syncytial viruses. Clinical Laboratory. 2021;67(6):1472-6.	Frozen samples used
Hwang SM, Lim MS, Han M, Hong YJ, Kim TS, Lee HR, et al. Comparison of xTAG respiratory virus panel and verigene respiratory virus plus for detecting influenza virus and respiratory syncytial virus. Journal of Clinical Laboratory Analysis. 2015;29(2):116-21.	Frozen samples used
Isles N, Badman SG, Ballard S, Zhang B, Howden BP, Guy R, et al. Analytical sensitivity and specificity of the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV assay. Pathology. 2022;54(1):120-2.	Wrong population
Jarrett J, Uhteg K, Forman MS, Hanlon A, Vargas C, Carroll KC, et al. Clinical performance of the GenMark Dx ePlex respiratory pathogen panels for upper and lower respiratory tract infections. Journal of Clinical Virology. 2021;135:104737.	Frozen samples used
Jee H, Park S, Lee J, Lim CS, Jang WS. Comparative Clinical Evaluation of a Novel FluA/FluB/SARS-CoV-2 Multiplex LAMP and Commercial FluA/FluB/SARS-CoV-2/RSV RT-qPCR Assays. Diagnostics. 2023;13(8):1432.	Not point of care
Jokela P, Vuorinen T, Waris M, Manninen R. Performance of the Alere i influenza A&B assay and mariPOC test for the rapid detection of influenza A and B viruses. Journal of Clinical Virology. 2015;70:72-6.	Unclear population and/or setting
Juretschko S, Mahony J, Buller RS, Manji R, Dunbar S, Walker K, et al. Multicenter clinical evaluation of the luminex aries flu A/B and RSV assay for pediatric and adult respiratory tract specimens. Journal of Clinical Microbiology. 2017;55(8):2431-8.	Wrong population

Kim J, Nam J, Jang W, Lim CS. Clinical Performance of the AllplexTM Respiratory Panel 1 Test Compared to SimplexaTM Flu A/B and RSV for Detection of Influenza Virus and Respiratory Syncytial Virus Infection Including Their Subtyping. Medical Principles and Practice. 2019;28(4):380-6.	Unclear population and/or setting
Kim SH, AlMutawa F. Tracheal Aspirate and Bronchoalveolar Lavage as Potential Specimen Types for COVID-19 Testing Using the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV. Microbiology Spectrum. 2022;10(3).	Wrong study design
Kim TY, Kim JY, Shim HJ, Yun SA, Jang JH, Huh HJ, et al. Comparison of the PowerChek SARS-CoV-2, Influenza A&B, RSV Multiplex Real-time PCR Kit and BioFire Respiratory Panel 2.1 for simultaneous detection of SARS-CoV-2, influenza A and B, and respiratory syncytial virus. Journal of Virological Methods. 2021;298:114304.	Frozen samples used
Ko SY, Jang JW, Song DJ, Lim CS, Kim WJ. Evaluation of the Simplexa Flu A/B and RSV test for the rapid detection of influenza viruses. Journal of Medical Virology. 2013;85(12):2160-4.	Unclear population and/or setting
Kosai K, Akamatsu N, Ota K, Mitsumoto-Kaseida F, Sakamoto K, Hasegawa H, et al. BioFire FilmArray Pneumonia Panel enhances detection of pathogens and antimicrobial resistance in lower respiratory tract specimens. Annals of Clinical Microbiology and Antimicrobials. 2022;21(1):24.	Frozen samples used
Kosai K, Kaku N, Horie M, Kodama H, Akamatsu N, Narita Y, et al. Clinical evaluation of a fully automated and high-throughput molecular testing system for detection of influenza virus. Virology Journal. 2022;19(1):188.	Frozen samples used
Lade H, Kim JM, Chung Y, Han M, Mo EK, Kim JS. Comparative evaluation of allplex respiratory panels 1, 2, 3, and biofire filmarray respiratory panel for the detection of respiratory infections. Diagnostics. 2022;12(1):9.	Unclear population and/or setting

Landry ML, Ferguson D. Comparison of Simplexa flu A/B & RSV PCR with cytospin- immunofluorescence and laboratory-developed TaqMan PCR in predominantly adult hospitalized patients. Journal of Clinical Microbiology. 2014;52(8):3057-9.	Frozen samples used
Leber AL, Everhart K, Daly JA, Hopper A, Harrington A, Schreckenberger P, et al. Multicenter evaluation of BioFire FilmArray respiratory panel 2 for detection of viruses and bacteria in nasopharyngeal swab samples. Journal of Clinical Microbiology. 2018;56(6).	Wrong population
Leber AL, Lisby JG, Hansen G, Relich RF, Schneider UV, Granato P, et al. Multicenter evaluation of the QIAstat-Dx respiratory panel for detection of viruses and bacteria in nasopharyngeal swab specimens. Journal of Clinical Microbiology. 2020;58(5):e00155-20.	Wrong population
Leonardi GP. Evaluation of Rapid, Molecular-Based Assays for the Detection of Respiratory Syncytial Virus. Intervirology. 2019;62(3):101-4.	Frozen samples used
Leung ECM, Chow VCY, Lee MKP, Tang KPS, Li DKC, Lai RWM. Evaluation of the Xpert Xpress SARS-CoV-2/Flu/RSV Assay for Simultaneous Detection of SARS-CoV-2, Influenza A and B Viruses, and Respiratory Syncytial Virus in Nasopharyngeal Specimens. Journal of Clinical Microbiology. 2021;59(4):e02965-20.	Frozen samples used
Li M, Brenwald N, Bonigal S, Chana K, Osman H, Oppenheim B. Rapid diagnosis of influenza: An evaluation of two commercially available RT-PCR assays. Journal of Infection. 2012;65(1):60-3.	Unclear population and/or setting
Lim HJ, Park JE, Park MY, Baek JH, Jung S, Sung N, et al. Assay system for simultaneous detection of sars-cov-2 and other respiratory viruses. Diagnostics. 2021;11(6):1084.	Frozen samples used
McIlwain DR, Chen H, Apkarian M, Affrime M, Bock B, Kim K, et al. Performance of BioFire array or QuickVue influenza A + B test versus a	Wrong population

validation qPCR assay for detection of influenza A during a volunteer A/California/2009/H1N1 challenge study. Virology Journal. 2021;18(1):45.	
McMullen P, Boonlayangoor S, Charnot-Katsikas A, Beavis KG, Tesic V. The performance of Luminex ARIES Flu A/B & RSV and Cepheid Xpert Flu/RSV XC for the detection of influenza A, influenza B, and respiratory syncytial virus in prospective patient samples. Journal of Clinical Virology. 2017;95:84-5.	Unclear population and/or setting
Mikamo H, Koizumi Y, Yamagishi Y, Asai N, Miyazono Y, Shinbo T, et al. Comparing the cobas Influenza A/B Nucleic acid test for use on the cobas Liat System (Liat) with rapid antigen tests for clinical management of Japanese patients at the point of care. PLoS ONE. 2022;17(10):e0276099.	Wrong population
Mitton B, Rule R, Said M. Laboratory evaluation of the BioFire FilmArray Pneumonia plus panel compared to conventional methods for the identification of bacteria in lower respiratory tract specimens: a prospective cross-sectional study from South Africa. Diagnostic Microbiology and Infectious Disease. 2021;99(2):115236.	Not point of care
Mostafa HH, Carroll KC, Hicken R, Berry GJ, Manji R, Smith E, et al. Multicenter evaluation of the cepheid xpert xpress SARS-CoV-2/Flu/RSV test. Journal of Clinical Microbiology. 2021;59(3):e02955-20.	Frozen samples used
Murphy CN, Fowler R, Balada-Llasat JM, Carroll A, Stone H, Akerele O, et al. Multicenter evaluation of the BioFire FilmArray Pneumonia/ Pneumonia plus panel for detection and quantification of agents of lower respiratory tract infection. Journal of Clinical Microbiology. 2020;58(7):e00128-20.	Wrong population
Nie S, Roth RB, Stiles J, Mikhlina A, Lu X, Tang YW, et al. Evaluation of alere i influenza A&B for rapid detection of influenza viruses A and B. Journal of Clinical Microbiology. 2014;52(9):3339-44.	Wrong population
Nolte FS, Gauld L, Barrett SB. Direct comparison of Alere i and cobas Liat influenza A and B tests for rapid detection of influenza virus infection. Journal of Clinical Microbiology. 2016;54(11):2763-6.	Wrong population

Novak-Weekley S, Marlowe EM, Poulter M, Dwyer D, Speers D, Rawlinson W, et al. Evaluation of the cepheid Xpert flu assay for rapid identification and differentiation of influenza A, influenza A 2009 H1N1, and influenza B viruses. Journal of Clinical Microbiology. 2012;50(5):1704-10.	Wrong population
Parcina M, Schneider UV, Visseaux B, Jozic R, Hannet I, Lisby JG. Multicenter evaluation of the QIAstat Respiratory Panel-A new rapid highly multiplexed PCR based assay for diagnosis of acute respiratory tract infections. PLoS ONE. 2020;15(3):e0230183.	Frozen samples used
Pedersen CJ, Rogan DT, Yang S, Quinn JV. Using a novel rapid viral test to improve triage of emergency department patients with acute respiratory illness during flu season. Journal of Clinical Virology. 2018;108:72-6.	Wrong population
Pichon M, Valette M, Schuffenecker I, Billaud G, Lina B. Analytical Performances of the Panther Fusion System for the Detection of Respiratory Viruses in the French National Reference Centre of Lyon, France. Microorganisms. 2020;8(9).	Wrong population
Popowitch EB, Kaplan S, Wu Z, Tang YW, Miller MB. Comparative Performance of the Luminex NxTAG Respiratory Pathogen Panel, GenMark eSensor Respiratory Viral Panel, and BioFire FilmArray Respiratory Panel. Microbiology Spectrum. 2022;10(4).	Frozen samples used
Popowitch EB, Miller MB. Comparison of the Xpert Flu/RSV XC and Xpress Flu/RSV assays. Journal of Clinical Microbiology. 2018;56(8):e00278-18.	Wrong population
Popowitch EB, O'Neill SS, Miller MB. Comparison of the biofire filmarray RP, Genmark eSensor RVP, Luminex xTAG RVPv1, and Luminex xTAG RVP fast multiplex assays for detection of respiratory viruses. Journal of Clinical Microbiology. 2013;51(5):1528-33.	Frozen samples used
Popowitch EB, Rogers E, Miller MB. Retrospective and prospective verification of the Cepheid Xpert influenza virus assay. Journal of Clinical Microbiology. 2011;49(9):3368-9.	Frozen samples used

Rabaan AA, Bazzi AM, Alshaikh SA. Comparison of Cepheid Xpert Flu and Roche RealTime Ready Influenza A/H1N1 Detection Set for detection of influenza A/H1N1. Diagnostic Microbiology and Infectious Disease. 2018;90(4):280-5.	Unclear population and/or setting
Regan J, Letant S, Adams K, Nguyen N, Derlet R, Cohen S, et al. A sample-in-answer-out instrument for the detection of multiple respiratory pathogens in unprepared nasopharyngeal swab samples. Analyst. 2010;135(9):2316-22.	Frozen samples used
Riazzo C, Perez-Ruiz M, Sanbonmatsu-Gamez S, Pedrosa-Corral I, Gutierrez-Fernandez J, Navarro-Mari JM. Analytical performance of the AlereTM i Influenza A&B assay for the rapid detection of influenza viruses. Enfermedades Infecciosas y Microbiologia Clinica. 2017;35(7):438-40.	Frozen samples used
Ruggiero P, McMillen T, Tang YW, Babady NE. Evaluation of the BioFire FilmArray Respiratory Panel and the GenMark eSensor Respiratory Viral Panel on Lower Respiratory Tract Specimens. Journal of Clinical Microbiology. 2014;52(1):288-90.	Frozen samples used
Salez N, Nougairede A, Ninove L, Zandotti C, de Lamballerie X, Charrel RN. Prospective and retrospective evaluation of the Cepheid Xpert Flu/RSV XC assay for rapid detection of influenza A, influenza B, and respiratory syncytial virus. Diagnostic Microbiology and Infectious Disease. 2015;81(4):256-8.	Wrong population
Sam SS, Caliendo AM, Ingersoll J, Abdul-Ali D, Hill CE, Kraft CS. Evaluation of performance characteristics of panther fusion assays for detection of respiratory viruses from nasopharyngeal and lower respiratory tract specimens. Journal of Clinical Microbiology. 2018;56(8):e00787-18.	Frozen samples used
Sambol AR, Iwen PC, Pieretti M, Basu S, Levi MH, Gilonske KD, et al. Validation of the Cepheid Xpert Flu A Real Time RT-PCR detection panel for Emergency Use Authorization. Journal of Clinical Virology. 2010;48(4):234-8.	Frozen samples used
Sanbonmatsu-Gamez S, Perez-Ruiz M, Lara-Oya A, Pedrosa-Corral I, Riazzo-Damas C, Navarro-Mari JM. Analytical performance of the automated	Wrong population

multianalyte point-of-care mariPOC for the detection of respiratory viruses. Diagnostic Microbiology and Infectious Disease. 2015;83(3):252-6.	
Sato Y, Nirasawa S, Saeki M, Yakuwa Y, Ono M, Kobayashi R, et al. Comparative study of rapid antigen testing and two nucleic acid amplification tests for influenza virus detection. Journal of Infection and Chemotherapy. 2022;28(7):1033-6.	Frozen samples used
Schmidt RLJ, Simon A, Popow-Kraupp T, Laggner A, Haslacher H, Fritzer-Szekeres M, et al. A novel PCR-based point-of-care method facilitates rapid, efficient, and sensitive diagnosis of influenza virus infection. Clinical Microbiology and Infection. 2019;25(8):1032-7.	No 2x2 data reported
Selvaraju SB, Bambach AV, Leber AL, Patru MM, Patel A, Menegus MA. Comparison of the SimplexaTM Flu A/B & RSV kit (nucleic acid extraction-dependent assay) and the Prodessa ProFlu+TM assay for detecting influenza and respiratory syncytial viruses. Diagnostic Microbiology and Infectious Disease. 2014;80(1):50-2.	Frozen samples used
Selvaraju SB, Tierney D, Leber AL, Patel A, Earley AK, Jaiswal D, et al. Influenza and respiratory syncytial virus detection in clinical specimens without nucleic acid extraction using FOCUS direct disc assay is substantially equivalent to the traditional methods and the FOCUS nucleic acid extraction-dependent RT-PCR assay. Diagnostic Microbiology and Infectious Disease. 2014;78(3):232-6.	Unclear population and/or setting
Serigstad S, Markussen D, Grewal HMS, Ebbesen M, Kommedal O, Heggelund L, et al. Rapid syndromic PCR testing in patients with respiratory tract infections reduces time to results and improves microbial yield. Scientific reports. 2022;12(1):326.	Wrong population
Shihabuddin BS, Faron ML, Relich RF, Van Heukelom P, Mayne D, Staat MA, et al. Cepheid Xpert Xpress Flu/RSV evaluation performed by minimally trained non-laboratory operators in a CLIA-waived environment. Diagnostic Microbiology and Infectious Disease. 2022;104(2):115764.	Wrong population

Sluimer J, Goderski G, van den Brink S, Broeders M, Rahamat-Langendoen J, Then E, et al. Multi-center evaluation of Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV molecular point-of-care test. Journal of Clinical Virology Plus. 2021;1(4):100042.	Frozen samples used
Sparks R, Balgahom R, Janto C, Polkinghorne A, Branley J. Verification of the BioFire FilmArray Pneumonia Plus Panel for pathogen screening of respiratory specimens. Pathology. 2021;53(7):919-22.	Wrong population
Steiner F, Schmutz S, Gosert R, Huder JB, Redli PM, Capaul R, et al. Usefulness of the GenMark ePlex RPP assay for the detection of respiratory viruses compared to the FTD21 multiplex RT-PCR. Diagnostic Microbiology and Infectious Disease. 2021;101(1):115424.	Frozen samples used
Stellrecht KA, Cimino JL, Wilson LI, Maceira VP, Butt SA. Panther Fusion Respiratory Virus Assays for the detection of influenza and other respiratory viruses. Journal of Clinical Virology. 2019;121:104204.	Wrong population
Stellrecht KA, Nattanmai SM, Butt J, Maceira VP, Espino AA, Castro AJ, et al. Effect of genomic drift of influenza PCR tests. Journal of Clinical Virology. 2017;93:25-9.	Wrong population
Svensson MJ, Lind I, Zweygberg Wirgart B, Rotzen Ostlund M, Albert J. Performance of the SimplexaTM Flu A/B & RSV Direct Kit on respiratory samples collected in saline solution. Scandinavian Journal of Infectious Diseases. 2014;46(12):825-31.	Wrong population
Sydenham TV, Bek-Thomsen M, Andersen SD, Kolmos B, Marmolin ES, Trebbien R, et al. Comparative evaluation of the CerTest VIASURE flu A, B & RSV real time RT-PCR detection kit on the BD MAX system versus a routine in-house assay for detection of influenza A and B virus during the 2016/17 influenza season. Journal of Clinical Virology. 2018;99:35-7.	Unclear population and/or setting
Teoh TK, Powell J, Kelly J, McDonnell C, Whelan R, O'Connell NH, et al. Outcomes of point-of-care testing for influenza in the emergency department	Wrong outcome

of a tertiary referral hospital in Ireland. Journal of Hospital Infection. 2021;110:45-51.	
To KKW, Yip CCY, Lai CYW, Wong CKH, Ho DTY, Pang PKP, et al. Saliva as a diagnostic specimen for testing respiratory virus by a point-of-care molecular assay: a diagnostic validity study. Clinical Microbiology and Infection. 2019;25(3):372-8.	Wrong population
Trombetta VK, Chan YL, Bankowski MJ. Are Rapid Influenza Antigen Tests Still Clinically Useful in Today's Molecular Diagnostics World? Hawai'i journal of medicine & public health : a journal of Asia Pacific Medicine & Public Health. 2018;77(9):226-30.	Unclear population and/or setting
Troppan KT, Bozic M, Santner BI, Kessler HH. Evaluation of four molecular assays for detection of pandemic influenza A (H1N1) 2009 virus in the routine diagnostic laboratory. Journal of Clinical Virology. 2010;49(2):82-4.	Frozen samples used
Van Der Westhuyzen M, Samodien N, Brink AJ, Moodley C. Utility of the BioFireFilmArrayPneumonia Panel plus assay for syndromic testing of lower respiratory tract infections in a low/middle-income setting. JAC-Antimicrobial Resistance. 2023;5(1):dlac139.	Wrong population
van Rijn AL, Nijhuis RHT, Bekker V, Groeneveld GH, Wessels E, Feltkamp MCW, et al. Clinical implications of rapid eplex respiratory pathogen panel testing compared to laboratory-developed real-time PCR. European Journal of Clinical Microbiology and Infectious Diseases. 2018;37(3):571-7.	No 2x2 data reported
Van Wesenbeeck L, Meeuws H, Van Immerseel A, Ispas G, Schmidt K, Houspie L, et al. Comparison of the FilmArray RP, verigene RV+, and prodesse ProFLU+/FAST+ multiplex platforms for detection of influenza viruses in clinical samples from the 2011-2012 influenza season in Belgium. Journal of Clinical Microbiology. 2013;51(9):2977-85.	Frozen samples used
Verbakel JY, Matheeussen V, Loens K, Kuijstermans M, Goossens H, Ieven M, et al. Performance and ease of use of a molecular point-of-care test for	Unclear population

influenza A/B and RSV in patients presenting to primary care. European Journal of Clinical Microbiology and Infectious Diseases. 2020;39(8):1453-60.	and/or setting
Voermans JJC, Mulders DGJC, Pas SD, Koopmans MPG, van der Eijk AA, Molenkamp R. Performance evaluation of the Panther Fusion respiratory tract panel. Journal of Clinical Virology. 2020;123:104232.	Frozen samples used
Voermans JJC, Seven-Deniz S, Fraaij PLA, van der Eijk AA, Koopmans MPG, Pas SD. Performance evaluation of a rapid molecular diagnostic, MultiCode based, sample-to-answer assay for the simultaneous detection of Influenza A, B and respiratory syncytial viruses. Journal of Clinical Virology. 2016;85:65-70.	Frozen samples used
Wabe N, Lindeman R, Post JJ, Rawlinson W, Miao M, Westbrook JI, et al. Cepheid Xpert Flu/RSV and Seegene AllplexTM RP1 show high diagnostic agreement for the detection of influenza A/B and respiratory syncytial viruses in clinical practice. Influenza and other Respiratory Viruses. 2021;15(2):245-53.	No 2x2 data reported
Wahrenbrock MG, Matushek S, Boonlayangoor S, Tesic V, Beavis KG, Charnot-Katsikas A. Comparison of cepheid xpert Flu/RSV XC and biofire filmarray for detection of influenza a, influenza b, and respiratory syncytial virus. Journal of Clinical Microbiology. 2016;54(7):1902-3.	Frozen samples used
Webber DM, Wallace MA, Burnham CAD, Anderson NW. Evaluation of the biofire filmarray pneumonia panel for detection of viral and bacterial pathogens in lower respiratory tract specimens in the setting of a tertiary care academic medical center. Journal of Clinical Microbiology. 2020;58(7):e00343-20.	Wrong population
Wolters F, Grunberg M, Huber M, Kessler HH, Pruller F, Saleh L, et al. European multicenter evaluation of Xpert Xpress SARS-CoV-2/Flu/RSV test. Journal of Medical Virology. 2021;93(10):5798-804.	Frozen samples used
Woodberry MW, Shankar R, Cent A, Jerome KR, Kuypers J. Comparison of the Simplexa FluA/B & RSV direct assay and laboratory-developed real-time	Unclear population

PCR assays for detection of respiratory virus. Journal of clinical microbiology. 2013;51(11):3883-5.	and/or setting
Yoo IY, Huh K, Shim HJ, Yun SA, Chung YN, Kang OK, et al. Evaluation of the BioFire FilmArray Pneumonia Panel for rapid detection of respiratory bacterial pathogens and antibiotic resistance genes in sputum and endotracheal aspirate specimens. International Journal of Infectious Diseases. 2020;95:326-31.	Frozen samples used
Young S, Illescas P, Nicasio J, Sickler JJ. Diagnostic accuracy of the real-time PCR cobas Liat Influenza A/B assay and the Alere i Influenza A&B NEAR isothermal nucleic acid amplification assay for the detection of influenza using adult nasopharyngeal specimens. Journal of Clinical Virology. 2017;94:86-90.	Wrong study design
Zafiropoulos A, Dermitzaki A, Malliarakis N, Stamataki M, Ergazaki M, Xenaki E, et al. Comparison of two point-of-care respiratory panels for the detection of influenza A/B virus. Infectious Diseases. 2023.	Wrong population
Zelyas N, Shokoples S, Droogers J, Lundeberg R, Leedell D, Drews SJ. Performance of the AlereTM i Influenza A&B and the Cepheid Xpert Flu/RSV XC assays. Future Virology. 2017;12(6):251-9.	Frozen samples used
Zhen W, Manji R, Smith E, Wuitschick J, Lucic D, Berry GJ. Evaluation of the Alinity m Resp-4-Plex Assay for the Detection of Severe Acute Respiratory Syndrome Coronavirus 2, Influenza A Virus, Influenza B Virus, and Respiratory Syncytial Virus. Microbiology Spectrum. 2022;10(1):e01090-21.	Frozen samples used
Zou X, Chang K, Wang Y, Li M, Zhang W, Wang C, et al. Comparison of the Cepheid Xpert Xpress Flu/RSV assay and commercial real-time PCR for the detection of influenza A and influenza B in a prospective cohort from China. International Journal of Infectious Diseases. 2019;80:92-7.	Wrong population