National Institute for Health and Care Excellence

Pneumonia: diagnosis and management (update)

[C] Evidence review for microbiological tests at presentation in secondary care to inform treatment decisions in people with suspected community or hospital acquired pneumonia.

NICE guideline [number]

Evidence reviews underpinning recommendations 1.4.5 to 1.4.7 and a research recommendation in the NICE guideline

April 2025

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1 Microbiological tests

1.1 Review question

What are the most effective and cost-effective microbiological tests or combination of tests at presentation in secondary care to inform treatment decisions in people with suspected community-acquired pneumonia or suspected hospital-acquired pneumonia?

1.1.1 Introduction

The various microbial causes of community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) are each sensitive or resistant to different antibiotics. Unfortunately, clinical, chest X-ray (CXR) and laboratory features do not allow accurate identification of the microbial cause in an individual patient. Empirical antibiotic therapy is usually commenced at patient presentation based on knowledge of likely pathogens. Targeting the correct antibiotic to the microbial cause in an individual patient is desirable. Traditional practice has been to send specimens (for example, of blood and or sputum) from each patient to the microbiology laboratory to try to identify the microbial cause in that patient and so refine the empirical antibiotic therapy. While a specific microbial cause is sometimes identified by this means, in the majority of cases no cause is found. The tests most commonly used are blood culture and sputum culture. Two urine antigen detection tests are also available in most hospitals. However, various factors can limit the clinical usefulness of these microbiological tests, and they have an associated cost. It is important to know which tests, or combination of tests, are clinically and cost-effective in managing treatment decisions in patients with CAP or HAP.

The aim of this review was to establish the efficacy and prognostic accuracy of various microbiological tests (including blood culture, sputum culture, urinary pneumococcal antigen, urinary legionella antigen) compared to clinical assessment alone to inform treatment decisions (including no treatment) for patients with suspected CAP or HAP, at presentation in secondary care.

1.1.2 Summary of the protocol

Table 1 PICOS inclusion criteria

Population	**Inclusion:** Babies over 28 days (corrected gestational age), children, young people (age <18 years) and adults (≥18 years) with pneumonia (community or hospital acquired) requiring management in hospital. • CAP is defined as pneumonia that is acquired outside hospital • HAP is defined as pneumonia that occurs 48 hours or more after hospital admission and is not incubating at hospital admission, or within 10 days of a previous hospital admission for a different problem.

	Note: studies that include a broader population (e.g. sepsis) will be included if: (a) they give results stratified for pneumonia; or (b) ≥ 75% patients have pneumonia. **Exclusion:** • Babies up to and including 28 days (corrected gestational age). • People with COVID-19 pneumonia. • People who acquire pneumonia while intubated (ventilator-associated pneumonia). • People who are severely immune-compromised (have a primary immune deficiency or secondary immune deficiency related to HIV infection, or severe drug or systemic disease-induced immunosuppression, for example, people who have taken immunosuppressant cancer therapy or undergone organ transplantation). • People in whom pneumonia is an expected terminal event. • People with non-pneumonic infective exacerbations of bronchiectasis. • People with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • People with pneumonia associated with cystic fibrosis. • People with aspiration pneumonia as a result of inhaling a large bolus of gastric contents.
Interventions	Microbiological tests, alone or in combination: - blood culture - sputum culture - urinary pneumococcal antigen - urinary legionella antigen - molecular testing of sputum or throat swab: o Single-plex o Multi-plex Note that due to the difficulty with obtaining sputum samples in children under 5, throat swabs or nasal swabs are more appropriate for this age group. Invasive sampling techniques (e.g. bronchoalveolar lavage and protected brush sampling) will not be considered as they are only applicable to a small proportion of the population.

Comparator	Usual care / clinical assessment alone
Outcomes	Primary outcomes: • Mortality within 30 days • Change in antibiotic and choice of antibiotic (broad or narrow spectrum) • Treatment duration • ICU admission • Need for invasive ventilation • Length of hospital stay • Length of ICU stay • Hospital re-admission within 30 days Secondary outcomes: • HRQoL (measured using validated tools such as the EQ5D or SF-36; or using condition-specific measures of QoL such as the CAP Symptom Questionnaire or the St George's Respiratory Questionnaire) • Adverse events e.g. hospital acquired infection, treatment side effects, C. diff, antimicrobial resistance, hospital infection outbreaks For test and treat RCTs, we will report outcome data for intervention and control groups. For prospective observational studies, we will use HRs, ORs and RRs. Where reported we will include • Sens/spec (converted to LR) • LR+/- • AUC
Study type	• Systematic reviews of RCTs and prognostic cohort studies • Test and treat RCTs • Prognostic cohort studies We will use a stepwise approach, so if insufficient test and treat RCTs or prospective studies (e.g. <5 good quality, directly relevant papers) then we will look at retrospective; but retrospective will be excluded if we identify enough test and treat RCTs or prospective studies.

AUC=area under the curve; CAP=community acquired pneumonia; HAP=hospital acquired pneumonia; HR=hazard ratio; HRQoL=health related quality of life; ICU=intensive care unit; OR=odds ratio; RCT=randomised controlled trials; RR=risk ratio

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 and the methods document.

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

1.1.3.1 Search methods

Each evidence review for this guideline had a search conducted in three parts. Part 1 was a single search for all systematic reviews relating to pneumonia published since 2014 that was screened for relevance to all the review questions. Part 2 was tailored to each evidence review. Part 3 covered the cost effectiveness elements of all review questions in a single search.

The searches for systematic reviews on all pneumonia topics were run on 20 November 2023 and re-run on 15 October 2024 in Cochrane Database of Systematic Reviews (CDSR) (Wiley) and Epistemonikos (https://www.epistemonikos.org).

The searches for effectiveness and prognostic evidence were run on 13 March 2024. The effectiveness searches were done in two parts so that different date limits could be applied to the appropriate population (adults since March 2014 and children and young people with no date limits).

The following databases were searched: Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley); Embase (Ovid); and MEDLINE ALL (Ovid). Limits were applied to remove animal studies, case reports, conference abstracts, editorials, empty registry entries, letters, news items and references not published in the English language. Validated NICE filters were used in MEDLINE and Embase to remove records exclusively set in countries that are not OECD members. Study-type filters were used in MEDLINE and Embase to limit to RCTs and prognostics.

The database searches were supplemented with additional search methods. Reference list checking and forward citation searching were conducted on Web of Science Core Collection on 12 March 2024 using seed references identified from the scoping searches, the papers included in CG191 and the search for systematic reviews.

The searches for cost effectiveness evidence were run on 20 November 2023 and re-run on 14 October 2024 for papers published since 2014. The following databases were searched: Econlit (Ovid); Embase (Ovid); International HTA Database (https://database.inahta.org); MEDLINE ALL (Ovid); and NHS Economic Evaluation Database (NHS EED) (CRD). The same limits as in the effectiveness search were used. The same limits as in the effectiveness search were used. The validated NICE Cost Utility Filter was used on MEDLINE and Embase. The NICE OECD filters were used in MEDLINE and Embase.

A NICE senior information specialist (SIS) conducted the searches. The MEDLINE strategy was quality assured by another NICE SIS and all translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2015 PRESS Guideline Statement.

Explanatory notes and full search strategies for each database are provided in appendix B.

1.1.4 Effectiveness and prognostic evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 4986 references (see appendix B for the literature search strategy).

These references were screened at title and abstract level against the review protocol, with 4943 excluded at this level. 10% of references were screened separately by two reviewers. Discrepancies were resolved by discussion.

The full texts of 43 were ordered for closer inspection. 6 of these studies met the criteria specified in the review protocol (appendix A). One further study was identified by the committee for inclusion. For a summary of the 7 included studies see table 2.

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 Excluded studies

Details of studies excluded at full text, along with reasons for exclusion are given in appendix J.

1.1.5 Summary of studies included in the evidence review

Table 2 Summary of studies included in the effectiveness evidence

Study details	Setting and location	Population	Intervention	Comparison	Risk of bias
New studies from this update					
Markussen 2024 N=374 Test and treat RCT	Setting: Hospital Location: Norway	Adult patients who presented to the ED with suspected CAP.	Rapid syndromic PCR testing (BioFire FilmArray Pneumonia plus Panel; bioMérieux) of LRT samples and standard of care. Treatment given according to test results.	Usual care: standard microbiological diagnostics alone. Treatment given according to test results.	Moderate
Virk 2024 N=1152 Test and treat RCT	Setting: Hospital Location: USA	Adult patients admitted to hospital with suspected pneumonia.	BioFire FilmArray pneumonia panel plus conventional culture and AST (antimicrobial susceptibility testing). Treatment given according to test results.	Usual care: Conventional culture and antimicrobial susceptibility testing. Treatment given according to test results.	Low
Studies included in previous evidence review					
Falguera 2010 N=194 test and treat RCT	Setting: Hospital Location: Spain	Adults with pneumonia of PSI class IV or V, or additional circumstances that justify hospital admission	Urinary antigen tests for S. pneumoniae and L. pneumophila. Treatment given according to test results.	Usual care: standard UK empiric treatment. Treatment given according to test results.	Moderate
Van der Eerden 2005 N=303 test and treat RCT	Setting: Hospital Location: Netherlands	Adults hospitalised with CAP	Combination of non-invasive and invasive tests including: • sputum for Gram stain and culture • S. pneumoniae antigen detection testing • blood culture • L. pneumophila serogroup 1 antigen detection	Usual care: standard beta-lactam plus macrolide tests. Treatment given according to test results.	Moderate

Study details	Setting and location	Population	Intervention	Comparison	Risk of bias
			• bronchoalveolar lavage specimen and protected specimen brush when no expectorated sputum or in case of clinical failure • thoracocentesis when pleural fluid was present • blood samples for serology (ELISA). Treatment given according to test results.		

ATS=American thoracic society; CAP=community acquired pneumonia; ED=emergency department; ELISA=enzyme-linked immunosorbent assay; LRT=lower respiratory tract; RCT=randomised controlled trial

See appendix D for full evidence tables

Table 3 Summary of studies included in the prognostic evidence

Study details	Setting/ and location	Population	Prognostic factors/ Prognostic model(s)	Outcomes investigated	Risk of bias
New studies from this update					
Cilloniz 2017 N= 278 Study type: Prospective cohort study	Setting: Hospital Location: Spain	Adults admitted to hospital with a diagnosis of community-acquired pneumococcal pneumonia	Positive blood culture for *Streptococcus pneumonia*	• in-hospital mortality • length of hospital stay • 30-day mortality • ICU admission	Moderate.

Study details	Setting/ and location	Population	Prognostic factors/ Prognostic model(s)	Outcomes investigated	Risk of bias
				• length of stay in ICU • ICU mortality • need of mechanical ventilation.	
Capelastegui 2014 N= 891 Study type: Prospective cohort study	Setting: Hospital Location: Spain	Adults diagnosed with and admitted to hospital with pneumococcal pneumonia.	Blood culture for streptococcus pneumoniae taken within 48 hours of presentation to the hospital	• in-hospital mortality • mortality at 15 and 30 days after admission • hospital readmission within 30 days • length of hospital stay	Moderate
Abelenda-Alonso 2022 N= 3677 Study type: Retrospective cohort study	Setting: Hospital Location: Spain	Non-immunosuppressed adults hospitalised with CAP	Positive blood culture.	• Antimicrobial de-escalation. • 30-day case-fatality rate • duration of antimicrobial intravenous (IV) therapy • total duration of antimicrobial therapy	Moderate

Study details	Setting/ and location	Population	Prognostic factors/ Prognostic model(s)	Outcomes investigated	Risk of bias
				• adverse events • length of hospital stay • CAP recurrence.	
Lee 2020 N= 1257 Study type: Retrospective cohort study	Setting: Hospital Location: Korea	Adult patients (aged ≥ 18 years) who were hospitalised with pneumonia	Pneumococcal urinary antigen test (PUAT)	• 30-day mortality	Moderate
Shen 2011 N=119 Study type: Retrospective cohort study	Setting: Hospital Location: Taiwan	Children with pneumococcal pneumonia who were hospitalised and had a positive pneumococcal urinary antigen test	Pneumococcal urinary antigen test (PUAT)	• ICU stay • Oxygen requirement • Intubation (mechanical ventilation) • Mortality	Serious
Studies included in previous evidence review					
Benenson 2007 Retrospective cohort	Setting: Hospital Location: USA	N=806 High severity adults hospitalised with CAP	Blood culture.	• mortality • change in treatment • length of stay	Moderate
Lidman 2002 Retrospective cohort	Setting: Hospital	N=605 High severity adults hospitalised with CAP	Combination of non-invasive and invasive tests including: • Blood culture (n = 418)	• mortality • change in treatment	High

Study details	Setting/ and location	Population	Prognostic factors/ Prognostic model(s)	Outcomes investigated	Risk of bias
	Location: Sweden		• Sputum culture (n = 182) • Serological analysis (n = 104); • Culture of pleural effusion (n = 9) • Protected brush specimens via bronchoscopy (n = 15).	• length of stay	
Piso 2012 Non-randomised comparative study	Setting: Emergency department Location: Switzerland	N=286 Moderate to high severity adults with CAP	Binax Now® pneumococcal antigen testing (PnAG) in addition to combination of tests including: • blood cultures • sputum cultures • urinary Binax Now® Legionella antigen testing (LgAG)	• change in treatment (within 48 to 72 hours of test)	Moderate
Dedier 2001 Retrospective cohort	Setting: Hospital Location: USA	N=1062 Adults hospitalised with CAP	• Blood culture within 24 hours of hospital arrival. • Blood culture before antibiotic administration.	• mortality (inpatient) • length of stay (> median) • clinical instability at 48 hours	Moderate
Lee 2011 Retrospective analysis of an RCT	Setting: Hospital Location: South Korea	N=2076 Adults hospitalised with CAP	Blood culture before antibiotics	• mortality 30 days after presentation • length of stay • hospital re-admission	Moderate

Study details	Setting/ and location	Population	Prognostic factors/ Prognostic model(s)	Outcomes investigated	Risk of bias
Meehan 1997 Retrospective cohort	Setting: Hospital Location: USA	N=14069 Older adults (>=65) hospitalised with pneumonia	Blood culture within 24 hours of hospital arrival Blood culture before antibiotic administration	• 30-day mortality	Moderate
Uematsu 2014 Retrospective cohort study using a multicentre claim-based inpatient database	Setting: Hospital Location: Japan	N=65,145 Adults hospitalised with CAP	• Sputum tests • Blood cultures • Urine antigen tests.	• 30 -day in - hospital mortality • length of hospital stay	High

CAP=community acquired pneumonia; ICU=intensive care unit; IV=intravenous; PnAG=pneumococcal antigen testing; PUAT=pneuomococcal urinary antigen testing; RCT=randomised controlled trial; TTP=thrombotic thrombocytopenic purpura

See appendix D for full evidence tables

1.1.6 Summary of the RCT evidence

Evidence from studies using PCR tests

Table 4: New evidence on positive rapid syndromic PCR testing of lower respiratory tract samples compared to negative testing for determining care in adults

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with negative testing	Risk with positive rapid syndromic PCR testing of lower respiratory tract samples				
Pathogen directed treatment based on test result within 48 h (CAP pts only)	155 per 1,000	**474 per 1,000** (289 to 780)	**RR 3.05** (1.86 to 5.02)	200 (1 RCT) [1]	⊕⊕◯◯ Low[a,b]	More likely with positive rapid PCR test
Readmission (CAP pts only)	184 per 1,000	**138 per 1,000** (65 to 293)	**RR 0.75** (0.35 to 1.59)	200 (1 RCT) [1]	⊕◯◯◯ Very low[a,b,c]	Could not differentiate
30-day mortality (CAP pts only)	39 per 1,000	**31 per 1,000** (7 to 141)	**RR 0.79** (0.17 to 3.62)	200 (1 RCT) [1]	⊕◯◯◯ Very low[a,b,c]	Could not differentiate
Length of stay	The median length of stay was **4** days	median **0.1 days fewer** (0 to 0)	-	200 (1 RCT) [1]	⊕⊕◯◯ Low[a,b]	No meaningful difference

CAP=community acquired pneumonia; CI=confidence interval; PCR=polymerase chain reaction; RCT=randomised controlled trial
a. Downgraded once as study at moderate risk of bias
b. Downgraded once as single study
c. Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
1. Markussen 2024

Table 5: New evidence on rapid syndromic PCR testing compared to standard care

Outcomes	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Mortality within 30 days	RR 0.79 (0.58 to 1.07)	414 (1RCT) [1]	Low[a,c]	Could not differentiate
Re-admission to hospital within 30 days	RR 0.77 (0.51 to 1.16)	514 (1RCT) [1]	Low[a,c]	Could not differentiate
Admission to ICU at 96 hours	0.39 (0.17 to 0.86)	166 (1RCT) [1]	Moderate[a]	Favours PCR test
Admission to ICU at 30 days	RR 0.61 (0.21 to 1.75)	166 (1RCT) [1]	Very low[a,b]	Could not differentiate
Change in antibiotics	RR 0.89 (0.81 to 0.98)	260 (1RCT) [1]	Moderate[a]	Favours PCR test

CI=confidence interval; ICU=intensive care unit; PCR=polymerase chain reaction; RCT=randomised controlled trial

a. Downgraded once as single study

b. Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)

c. Downgraded once as CI crosses one clinical threshold (0.8 or 1.25)

1. Virk 2024

1.1.6 Summary of the mixed RCT and observational evidence

Evidence from studies using combinations of tests

Table 6: Existing evidence from the previous review on targeted treatment using a combination of tests compared with standard care

Outcome	Studies	N of patients		Effect		Quality
		PUAT test targeted treatment	Standard care	Relative (95% CI)	Absolute	
Mortality (follow-up 30 days)	1 (van der Eerden 2005)	12/152 (14.6%)	22/151 (14.6%)	RR 0.54 (0.28 to 1.06)	67 fewer per 1000 (from 105 fewer to 9 more)	Very low[2]
Mortality (follow-up 3 months)	1 (Lidman 2002)	42/482 (8.7%)	29/123 (23.6%)	RR 0.37 (0.24 to 0.57)	149 fewer per 1000 (from 101 fewer to 179 fewer)	Very low[2]
Mortality (30-day in-hospital)	1 ([Uematsu 2014)	-	-	AOR 0.64 (0.56 to 0.74)[1]	-	Very low[2]
Clinical failure (follow-up 30 days)	1 (van der Eerden 2005)	32/152 (21.1%)	35/151 (23.2%)	RR 0.91 (0.59 to 1.39)	21 fewer per 1000 (from 95 fewer to 90 more)	Very low[2]
Length of hospital stay	1 (van der Eerden 2005)	14.3 (9.4)	13.2 (13.2)	-	MD 1.1 higher (1.48 lower to 3.68 higher)	Low[3]
Length of hospital stay	1 (Lidman 2002)	5 (1 to 90)	5 (1 to 34)	-	-	Very low[2]
Length of hospital stay (time to hospital discharge)	1 ([Uematsu 2014)	-	-	AHR 1.04 (1.00 to 1.07)	-	Very low[2]
Quality-of-life; SF-36 - 30 days (follow-up 30 days)	1 (van der Eerden 2005)	59.5 (21.5)	57.3 (20.5)	-	MD 2.2 higher (5.48 lower to 9.88 higher)	Very low[2]
Quality-of-life; SF-36 - 90 days (follow-up 90 days)	1 (van der Eerden 2005)	66.7 (22.9)	67.2 (30.1)	-	MD 0.5 lower (12.32 lower to 11.32 higher)	Low[3]
Quality-of-life; SF-36 - 180 days (follow-up 180 days)	1 (van der Eerden 2005)	79.3 (22.4)	64.1 (20.1)	-	MD 15.2 higher (3.68 to 26.72 higher)	Very low[2]

Change in prescription (based on test results)	1 (van der Eerden 2005)	25/134 (18.7%)	0/128 (0%)	PETO OR 8.61 (3.78 to 19.61)	190 (120 more per 1000 to 250 more	Low[3]
Change in prescription (based on test results or clinical judgement)	1 (Lidman 2002)	133/482 (27.6%)	23/123 (18.7%)	RR 1.48 (0.99 to 2.19)	90 more per 1000 (from 2 fewer to 223 more)	Very low[2]

AHR=adjusted hazard ratio; AOR=adjusted odds ratio; CI=confidence interval; PUAT=pneumococcal urinary antigen test; RR=risk ratio
1 Multivariate analysis adjusted for age, sex, orientation disturbance, respiratory failure, low blood pressure, dehydration, comorbidities, emergency admission via ambulance, use of intensive care units, university-affiliated major hospital status, treatment in a pulmonary unit, hospital volume, and hospital size and doctor-to-bed and nurse-to-bed ratios
2 Downgraded twice for risk of bias and once for indirectness
3 Downgraded once for risk of bias and once for indirectness

Table 7: Existing evidence from the previous review on outcomes for different combination of tests compared with no test stratified by severity status (Uematsu 2014)

Severity strata[1]	30-day in hospital mortality - Adjusted odds ratio (95% CI)	Length of stay (time to hospital discharge) Adjusted hazard ratio (95% CI)	Quality
Comparison of combination of tests with no test			
Mild	AOR 1.08 (0.36 to 3.26)	AHR 0.95 (0.89 to 1.02)	Very low[2]
Moderate	AOR 0.83 (0.66 to 1.04)	AHR 1.02 (0.98 to 1.07)	Very low[2]
Severe	AOR 0.70 (0.54 to 0.91)	AHR 1.12 (1.03 to 1.22)	Very low[2]
Very severe	AOR 0.51 (0.40 to 0.64)	AHR 1.12 (1.01 to 1.23)	Very low[2]
Comparison of blood cultures with no test			
Mild	AOR 1.67 (0.79 to 3.53)	AHR 0.92 (0.88 to 0.97)	Very low[2]
Moderate	AOR 0.79 (0.68 to 0.93)	AHR 1.03 (1.00 to 1.05)	Very low[2]
Severe	AOR 0.71 (0.60 to 0.85)	AHR 1.05 (0.99 to 1.12)	Very low[2]
Very severe	AOR 0.81 (0.70 to 0.93)	AHR 1.02 (0.95 to 1.09)	Very low[2]
Comparison of urinary antigen tests with no test			
Mild	AOR 0.39 (0.16 to 0.99)	AHR 1.03 (0.98 to 1.07)	Very low[2]
Moderate	AOR 0.80 (0.69 to 0.94)	AHR 1.07 (1.04 to 1.10)	Very low[2]
Severe	AOR 0.75 (0.63 to 0.89)	AHR 1.05 (0.99 to 1.11)	Very low[2]
Very severe	AOR 0.75 (0.64 to 0.87)	AHR 1.15 (1.08 to 1.24)	Very low[2]
Comparison of sputum tests with no test			

Mild	OR 1.00 (0.50 to 2.00)	AHR 0.98 (0.94 to 1.01)	Very low[2]
Moderate	AOR 1.11 (0.98 to 1.26)	AHR 0.97 (0.95 to 0.99)	Very low[2]
Severe	AOR 1.22 (1.05 to 1.41)	AHR 1.02 (0.97 to 1.08)	Very low[2]
Very severe	AOR 0.93 (0.82 to 1.05)	AHR 1.01 (0.95 to 1.07)	Very low[2]

AHR=adjusted hazard ratio; AOR=adjusted odds ratio; CI=confidence interval

1 Severity was assessed based on the A-DROP severity assessment tool

2 Retrospective database analysis, post-hoc subgroup analysis. Length of stay in Japan and UK may be different, limiting applicability of findings

1.1.6 Summary of the prognostic evidence

Evidence for studies using blood culture tests

Table 8: New evidence of positive blood culture compared to negative blood culture for making care decisions in adults

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with negative blood culture	Risk with positive blood culture				
Admission to ITU - Stretococcus pneumoniae bacteremia	205 per 1,000	**230 per 1,000** (181 to 296)	**RR 1.12** (0.88 to 1.44)	891 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a,b]	Could not differentiate
Admission to ITU - Any positive blood culture	48 per 1,000	**130 per 1,000** (103 to 166)	**RR 2.72** (2.14 to 3.46)	3677 (1 non-randomised study) [2]	⨁◯◯◯ Very low[a]	More likely with positive blood culture

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with negative blood culture	Risk with positive blood culture				
Need for mechanical ventilation (Stretococcus pneumoniae bacteremia)	55 per 1,000	**105 per 1,000** (66 to 167)	**RR 1.92** (1.20 to 3.05)	891 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b]	More likely with positive blood culture
Treatment failure (Stretococcus pneumoniae bacteremia)	120 per 1,000	**180 per 1,000** (132 to 248)	**RR 1.50** (1.10 to 2.07)	891 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b]	More likely with positive blood culture
In hospital mortality (Stretococcus pneumoniae bacteremia)	45 per 1,000	**88 per 1,000** (52 to 147)	**RR 1.96** (1.17 to 3.29)	891 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b]	More likely with positive blood culture
30-day mortality (Stretococcus pneumoniae bacteremia)	37 per 1,000	**93 per 1,000** (54 to 160)	**RR 2.53** (1.47 to 4.38)	891 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a]	More likely with positive blood culture
30-day readmission (Stretococcus pneumoniae bacteremia)	55 per 1,000	**25 per 1,000** (12 to 51)	**RR 0.46** (0.22 to 0.93)	891 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,c]	Less likely with positive blood culture

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with negative blood culture	Risk with positive blood culture				
Hospital stay <3 days (Stretococcus pneumoniae bacteremia)	758 per 1,000	**743 per 1,000** (682 to 796)	**RR 0.98** (0.90 to 1.05)	891 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a]	No meaningful difference
Length of hospital stay (Stretococcus pneumoniae bacteremia) [MID 2.75)	The mean length of hospital stay (Stretococcus pneumoniae bacteremia) [MID 2.75) was 7 days	MD **3 days more** (1.57 more to 4.43 more)	-	891 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,d]	Longer with positive blood culture
Antimicrobial de-escalation (any positive blood culture)	102 per 1,000	**337 per 1,000** (289 to 392)	**RR 3.30** (2.83 to 3.84)	3677 (1 non-randomised study) [2]	⊕◯◯◯ Very low[a,e]	More likely with positive blood culture

CI=confidence interval; MD=mean deviation; MID=minimal important difference; RR=risk ratio; ITU=intensive therapy unit
a. Downgraded once as single study
b. Downgraded once as 95% CI crosses one clinical decision threshold (1.25)
c. Downgraded once as 95% CI crosses one clinical decision threshold (0.8)
d. Downgraded once as 95% CI crosses one clinical decision threshold (2.75)
e. Downgraded once for moderate risk of bias
1. Capelastegui (2014)
2. Abelenda (2022)

Table 9: New evidence on early blood culture positivity compared to late blood culture positivity for planning care in streptococcus pneumoniae bacteraemia in adults

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with late blood culture positivity	**Risk with early blood culture positivity**				
Length of stay <= 9 days	440 per 1,000	**682 per 1,000** (546 to 850)	**RR 1.55** (1.24 to 1.93)	278 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,c]	More likely with early positive culture
In hospital mortality	43 per 1,000	**145 per 1,000** (62 to 342)	**RR 3.37** (1.43 to 7.94)	278 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b]	More likely with early positive culture
30-day mortality	53 per 1,000	**145 per 1,000** (64 to 326)	**RR 2.75** (1.22 to 6.20)	278 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,c]	More likely with early positive culture
ICU admission	287 per 1,000	**390 per 1,000** (273 to 563)	**RR 1.36** (0.95 to 1.96)	278 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,c]	Could not differentiate
ICU mortality	19 per 1,000	**58 per 1,000** (15 to 226)	**RR 3.03** (0.78 to 11.79)	278 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,d]	Could not differentiate
Need for mechanical ventilation	53 per 1,000	**159 per 1,000** (72 to 352)	**RR 3.03** (1.37 to 6.68)	278 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b]	More likely with early positive culture

CI=confidence interval; ICU=intensive care unit; RR=risk ratio
a. Downgraded once for moderate risk of bias
b. Downgraded once for inconsistency: single study
c. Downgraded once as CI crosses one clinical threshold (1.25)
d. Downgraded twice as CI crosses two clinical threshold (0.8-1.25)

1. Cilloniz (2017)

Table 10: Existing evidence from the previous review on targeted treatment using blood culture compared with standard care

Outcome	Studies	N of patients		Effect		Quality
		Blood culture targeted treatment	Standard care	Relative (95% CI)	Absolute	
Mortality (follow-up unclear)	1 (Benenson 2007)	32/667 (4.8%)	8/118 (6.8%)	RR 0.71 (0.33 to 1.5)	20 fewer per 1000 (from 45 fewer to 34 more)	Very low[5]
Mortality (30-day in-hospital)	1 (Uematsu 2014)	-	-	AOR 0.78 (0.71 to 1.40)[1]	-	Very low[5]
Mortality (in-hospital) - Blood culture within 24 hours	1 (Dedier 2001)	54/841 (6.4%)	5/150 (3.3%)	AOR 0.86 (0.36 to 2.05)[2]	-	Very low[6]
Mortality (in-hospital) - Blood culture before antibiotic therapy	1 (Dedier 2001)	-	-	AOR 1.21 (0.62 to 2.36)[2]	-	Very low[6]
Mortality (30-day) - Blood culture before antibiotic therapy	2 (Lee 2011; Meehan 1997)	-	-	AOR 0.92 (0.82 to 1.02)[3] AOR 0.90 (0.60 to 1.30)[4]	-	Very low[7]
Mortality (30-day) – Blood culture within 24 hours	1 (Meehan 1997)	4502	9567	AOR 0.90 (0.81 to 1.00)[3]	-	Very low[8]
Clinical instability at 48 hours - Blood culture within 24 hours	1 (Dedier 2001)	186	876	AOR 1.62 (1.13 to 2.32)[2]	-	Very low[6]
Clinical instability at 48 hours - Blood culture before antibiotic therapy	1 (Dedier 2001)	294	768	AOR 1.06 (0.74 to 1.52)[2]	-	Very low[7]
Length of hospital stay	1 (Benenson 2007)	5.3 (3.4)	5 (4.3)	-	MD 0.3 higher (0.52 lower to 1.12 higher)	Very low[8]
Length of hospital stay (longer than median 4 days) - Blood culture within 24 hours	1 (Dedier 2001)	-	-	AOR 1.04 (0.72 to 1.50)[2]	-	Very low[7]

Length of hospital stay (longer than median 4 days) - Blood culture before antibiotic therapy	1 (Dedier 2001)	-	-	AOR 0.84 (0.60 to 1.18) [2]	-	Very low[6]
Length of hospital stay - Blood culture before antibiotic therapy	1 (Lee 2011)	Median 5 (3 to 7)	Median 5 (3 to 8)	AHR 1 (0.90 to 1.20) [4]	-	Very low[9]
Length of hospital stay (time to hospital discharge)	1 (Utematsu 2014)	-	-	AHR 1.00 (0.98 to 1.02) [1]	-	Very low[8]
Hospital re-admission - Blood culture before antibiotic therapy	1 (Lee 2011)	-	-	AOR 0.80 (0.60 to 1.07) [4]	-	Very low[6]
Change in treatment based on test results	1 (Benenson 2007)	3/684 (0.4%)	0/122 (0%)	PETO OR 3.26 (0.14 to 76.9)	0 more per 1000 (from 10 fewer to 10 more)	Very low[10]

AHR=adjusted hazard ratio; AOR=adjusted odds ratio; CI=confidence interval; OR=odds ratio; RR=risk ratio

1 Multivariate analysis adjusted for age, sex, orientation disturbance, respiratory failure, low blood pressure, dehydration, comorbidities, emergency admission via ambulance, use of intensive care units, university-affiliated major hospital status, treatment in a pulmonary unit, hospital volume, and hospital size and doctor-to-bed and nurse-to-bed ratios

2 Multivariate analysis adjusted for antibiotics administration ≤ 8 hours of hospital arrival, blood culture ≤ 24 hours, blood culture before antibiotics, oxygenation measurement ≤ 24 hours, and PSI

3 Multivariate analysis adjusted for time from hospital arrival to initial antibiotic administration, blood culture prior to initial antibiotic, blood culture within 24 hours of arrival, oxygenation assessment within 24 hours of arrival, demographics (age, sex, nursing home residence), comorbidities (cerebrovascular disease, congestive heart failure, neoplastic disease), physical examination findings, lab/test results

4 Multivariate analysis adjusted for PSI risk class, age, guideline implementation (low, moderate or high intensity), nursing home residence, physical examination findings, lab and radiographic findings, treatments before presentation, comorbidities not contained in the PSI – cognitive impairment, history of coronary artery disease, chronic pulmonary disease, diabetes

5 Downgraded twice for risk of bias, once for indirectness and twice for imprecision (95% CI crosses both default MIDs)

6 Downgraded once for risk of bias, once for indirectness and once for imprecision (95% CI crosses 1 default MID)

7 Downgraded once for risk of bias, once for indirectness and twice for imprecision (95% CI crosses both default MIDs)

8 Downgraded twice for risk of bias and once for indirectness

9 Downgraded once for risk of bias and once for indirectness

10 Downgraded once for risk of bias, twice for indirectness and twice for imprecision (95% CI crosses both default MIDs)

Evidence from studies using sputum culture tests

Table 11: Existing evidence from the previous review on targeted treatment using sputum culture compared with standard care

Outcome	Studies	N of patients		Effect		Quality
		PUAT test targeted treatment	Standard care	Relative (95% CI)	Absolute	
Mortality (30-day in-hospital)	1 (Uematsu 2014)			AOR 1.06 (0.98 to 1.15)[1]		Very low[2]
Length of hospital stay (time to hospital discharge)	1 (Uematsu 2014)			AHR 0.98 (0.97 to 1.00)[1]		Very low[2]

AHR=adjusted hazard ratio; AOR=adjusted odds ratio; CI=confidence interval

1 Multivariate analysis adjusted for age, sex, orientation disturbance, respiratory failure, low blood pressure, dehydration, comorbidities, emergency admission via ambulance, use of intensive care units, university-affiliated major hospital status, treatment in a pulmonary unit, hospital volume, and hospital size and doctor-to-bed and nurse-to-bed ratios

2 Downgraded twice for risk of bias and once for indirectness

Evidence from studies using pneumococcal urinary antigen tests

Table 12: New evidence on positive pneumococcal urinary antigen test (PUAT) compared to negative PUAT for determining care in adults

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with negative PUAT	**Risk with positive pneumococcal urinary antigen test (PUAT)**				
Length of hospital stay - Full cohort [MID: 4.4]	The mean length of hospital stay - Full cohort was **9.6** days	MD **1.2 days more** (0.71 fewer to 3.11 more)	-	1257 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b]	No meaningful difference
Length of hospital stay - Propensity score matched [MID: 5.25]	The mean length of hospital stay - Propensity score matched] was **12.3** days	MD **1.4 days fewer** (3.87 fewer to 1.07 more)	-	322 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b]	No meaningful difference
Duration of antibiotic therapy - Full cohort [MID: 4.1]	The mean duration of antibiotic therapy - Full cohort was **11.6** days	MD **0.5 days fewer** (1.54 fewer to 0.54 more)	-	1257 (1 non-randomised study) [1]	⨁◯◯◯ Very low[b]	No meaningful difference
Duration of antibiotic therapy - Propensity score matched [3.35]	The mean duration of antibiotic therapy - Propensity score matched was **11.9** days	MD **0.8 days fewer** (2.19 fewer to 0.59 more)	-	322 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b]	No meaningful difference

CI=confidence interval; MD=mean difference; MID=minimal important difference; PUAT=pneumococcal urinary antigen test; RR=risk ratio

a. Downgraded once for moderate risk of bias
b. Downgraded once for single study
1. Lee 2020

Table 13: New evidence on positive pneumococcal urinary antigen test (PUAT) compared to negative PUAT for determining care in children

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with negative PUAT	**Risk with positive pneumococcal urinary antigen test (PUAT)**				
Antigen reactivity score 8 vs. score 5-7						
Admission to ITU	477 per 1,000	**749 per 1,000** (525 to 1,000)	**RR 1.57** (1.10 to 2.25)	84 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,c]	More likely with score 8
Require oxygen therapy	341 per 1,000	**651 per 1,000** (406 to 1,000)	**RR 1.91** (1.19 to 3.05)	84 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,c]	More likely with score 8
Invasive mechanical ventilation	23 per 1,000	**200 per 1,000** (26 to 1,000)	**RR 8.80** (1.15 to 67.29)	84 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,c]	More likely with score 8
Mortality	0 per 1,000	**0 per 1,000** (0 to 0)	**RR 3.29** (0.14 to 78.59)	84 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b,c]	Could not differentiate
Antigen reactivity score 8 vs. score 2-4						
Admission to ITU	286 per 1,000	**751 per 1,000** (431 to 1,000)	**RR 2.63** (1.51 to 4.57)	75 (1 non-randomised study) [1]	⊕◯◯◯ Very low[a,b]	More likely with score 8

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
	Risk with negative PUAT	**Risk with positive pneumococcal urinary antigen test (PUAT)**				
Require oxygen therapy	143 per 1,000	**650 per 1,000** (280 to 1,000)	**RR 4.55** (1.96 to 10.57)	75 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b]	More likely with score 8
Invasive mechanical ventilation	57 per 1,000	**200 per 1,000** (46 to 880)	**RR 3.5** (0.8 to 15.4)	75 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b,d]	Could not differentiate
Mortality	29 per 1,000	**25 per 1,000** (2 to 385)	**RR 0.88** (0.06 to 13.48)	75 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b,c]	Could not differentiate
Antigen reactivity score 5-7 vs. score 2-4						
Admission to ITU	286 per 1,000	**477 per 1,000** (260 to 877)	**RR 1.67** (0.91 to 3.07)	79 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b,c]	Could not differentiate
Require oxygen therapy	143 per 1,000	**341 per 1,000** (137 to 847)	**RR 2.39** (0.96 to 5.93)	79 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b,c]	Could not differentiate
Invasive mechanical ventilation	57 per 1,000	**23 per 1,000** (2 to 241)	**RR 0.40** (0.04 to 4.21)	79 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b,c]	Could not differentiate
Mortality	29 per 1,000	**8 per 1,000** (0 to 181)	**RR 0.27** (0.01 to 6.35)	79 (1 non-randomised study) [1]	⨁◯◯◯ Very low[a,b,c]	Could not differentiate

1 CI=confidence interval; ITU=intensive therapy unit; PUAT=pneumococcal urinary antigen test; RR=risk ratio

a. Single study at serious risk of bias
b. Downgraded once for single study.
c. Downgraded once for crossing one clinical decision threshold (1.25)
d. Downgraded twice for crossing both clinical decision thresholds (0.8 and 1.25)
1. Shen 2011

Table 14: Existing evidence from the previous review on targeted treatment using urinary antigen tests compared with standard care

Outcome	Studies	N of patients		Effect		Quality
		PUAT test targeted treatment	Standard care	Relative (95% CI)	Absolute	
Mortality (follow-up 30 days after treatment)	1 (Falguera 2010)	1/88 (1.1%)	0/89 (0%)	PETO OR 7.47 (0.15 to 376.66)	10 more (20 fewer per 1000 to 40 more)	Very low[2]
Mortality (30-day in-hospital)	1 (Uematsu 2014)	-	-	AOR 0.75 (0.69 to 0.82) [1]	-	Very low[3]
Clinical relapse (follow-up up to 30 days after discharge)	1 (Falguera 2010)	4/88 (4.5%)	2/89 (2.2%)	RR 2.02 (0.38 to 10.76)	23 more per 1000 (from 14 fewer to 219 more)	Very low[2]
Re-admission (follow-up up to 30 days after discharge)	1 (Falguera 2010)	4/88 (4.5%)	2/89 (2.2%)	RR 2.02 (0.38 to 10.76)	23 more per 1000 (from 14 fewer to 219 more)	Very low[2]
Treatment withdrawal due to adverse events (follow-up 5 to 10 days)	1 (Falguera 2010)	1/88 (1.1%)	1/89 (1.1%)	RR 1.01 (0.06 to 15.92)	0 more per 1000 (from 11 fewer to 168 more)	Very low[2]
Length of hospital stay	1 (Falguera 2010)	7.1 (4)	7.1 (3.8)	-	MD 0 higher (1.15 lower to 1.15 higher)	Low[4]
Length of hospital stay (assessed by hospital discharge)	1 (Uematsu 2014)	-	-	AHR 1.07 (1.05 to 1.10) [1]	-	Very low[5]

AHR=adjusted hazard ratio; AOR; adjusted odds ratio; CI=confidence interval; PUAT=pneumococcal urinary antigen test; RR=risk ratio

1 Multivariate analysis adjusted for age, sex, orientation disturbance, respiratory failure, low blood pressure, dehydration, comorbidities, emergency admission via ambulance, use of intensive care units, university-affiliated major hospital status, treatment in a pulmonary unit Hospital volume, and hospital size and doctor-to-bed and nurse-to-bed ratios
2 Downgraded once for risk of bias, once for indirectness and twice for imprecision
3 Downgraded twice for risk of bias, once for indirectness and once for imprecision
4 Downgraded once for risk of bias and once for indirectness
5 Downgraded twice for risk of bias and once for indirectness

Table 45: Existing evidence from the previous review on targeted treatment following urinary pneumococcal antigen compared with targeted treatment not using

Outcome	Studies	N of patients		Effect		Quality
		PUAT test targeted treatment	Standard care	Relative (95% CI)	Absolute	
Change in prescription (within 48 to 72 hours)	1 (Piso 2012)	88/139 (63.3%)	80/147 (54.4%)	RR 1.16 (0.96 to 1.41)	87 more per 1000 (from 22 fewer to 223 more)	Very low[1]

CI=confidence interval; PUAT=pneumococcal urinary antigen test; RR=risk ratio
1 Downgraded once for risk of bias and once for imprecision

See appendix F for full GRADE tables.

1.1.7 Economic evidence

1.1.7.1 Included studies

A single search was performed to identify published economic evaluations of relevance to any of the questions in this guideline update. See **Error! Reference source not found.**for the search strategy.

This search retrieved 3,201 studies. Based on title and abstract screening, 3,168 of the studies could confidently be excluded for this question. A single de novo modelling study from the previous iteration of the guideline was also included in this review question. Thirty-two studies were excluded following the full-text review. See **Error! Reference source not found.**for the study selection process.

Two studies were included in this review. These are summarised in the economic evidence summary tables below (**Error! Reference source not found.** and **Error! Reference source not found.**) and the economic evidence tables in Appendix H – Economic evidence tables.

1.1.7.2 Excluded studies

See **Error! Reference source not found.** for a full list of excluded studies, with reasons for exclusions

1.1.8 Summary of included economic evidence

Table 5 Economic evidence summary table: Urine antigen test and blood and sputum culture vs blood and sputum culture alone

Study	Applicability and limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Xie 2017 Canada	Partly applicable[a] Potentially serious[b]	• Cost effectiveness	£27.77	Proportion of patients correctly classified: 0.062	£449.05 per person correctly classified	The cost of the urine antigen test was the main driver of the model. The prevalence of streptococcus pneumoniae and the cost of antibiotics had little effect on the cost effectiveness.

(a) Canadian study based on a single tertiary care hospital in Montreal, cost effectiveness study rather than a cost utility study
(b) Expert assumptions used for baseline outcomes. Single hospital perspective rather than national.

Table 6 Economic evidence summary table: Multiple interventions

Study	Applicability and limitations	Other comments	Total costs (£)	Total effects (QALYs)	Cost effectiveness NMB (QALY*20000-£)	Uncertainty
CG191 (2014) UK	Directly applicable Potentially serious[a]	Interventions: [1] no testing (clinical judgement) [2] blood culture [3] sputum culture [4] urinary pneumococcal antigen	[1] £2,570 [2] £2,582 [3] £2,664 [4] £2,589 [5] £2,610	[1] 7.349 [2] 7.367 [3] 7.407 [4] 7.349 [5] 7.349	[1] £144,406 [2] £144,758 [3] £145,468 [4] £144,387 [5] £144,366	Multiple inputs were assessed in sensitivity analyses including changing mortality assumptions, removing sputum culture from the model, changing the prevalence of pathogens, changing the quality-of-

Study	Applicability and limitations	Other comments	Total costs (£)	Total effects (QALYs)	Cost effectiveness NMB (QALY*20000-£)	Uncertainty
		[5] urinary legionella antigen [6] combination of a blood culture and a sputum culture [7] combination of a blood culture, a urinary pneumococcal antigen and a urinary legionella antigen [8] all tests in combination	[6] £2,683 [7] £2,642 [8] £2,731	[6] 7.410 [7] 7.367 [8] 7.410	[6] £145,524 [7] £144,698 [8] £145,475	life assumptions, reducing the test sensitivities. Several sensitivity analyses on mortality assumptions, prevalence of pathogens, and quality-of-life assumptions showed that the combination of all tests was the most cost-effective strategy. However, in the majority of the sensitivity analyses, the combination of a blood culture and a sputum culture remained the preferred strategy.

Abbreviations: QALY: Quality-Adjusted Life-Years; UK: United Kingdom; NMB: Net Monetary Benefit
(a) Multiple model inputs were based on committee assumptions including the sensitivity and specificity of tests, mortality, cost of test

1.1.9 Economic model

Whilst this review question was prioritised for modelling there was a lack of available data. Therefore, no original health economic modelling was done for this review question.

1.1.10 Unit costs

Since cost-utility modelling was not feasible, the committee was provided with unit cost data to help them assess the potential impact on costs and cost-effectiveness when making their recommendations.

Table 7 Unit costs

Resource	Unit costs	Source
Blood culture	£31.46[a]	GC191
Sputum culture	£25.71[a]	GC191
Urinary legionella antigen (sent to laboratory)	£53.08[a]	GC191
Urinary pneumococcal antigen (sent to laboratory)	£53.08[a]	GC191
Urinary antigen test (not sent to laboratory)	£20	Committee expert opinion
Molecular assay	£150	Committee expert opinion

(a) Costs uprated from 2014 to 2024 using CCEMG - EPPI-Centre Cost Converter v.1.4 (ioe.ac.uk)

1.1.14 References – included studies

1.1.14.1 Effectiveness and prognostic evidence

Abelenda-Alonso, Gabriela, Rombauts, Alexander, Gudiol, Carlota et al. (2022) Effect of positive microbiological testing on antibiotic de-escalation and outcomes in community-acquired pneumonia: a propensity score analysis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 28(12): 1602-1608

Benenson RS, Kepner AM, Pyle DN, Cavanaugh S. Selective use of blood cultures in emergency department pneumonia patients. Journal of Emergency Medicine. 2007; 33(1):1-8

Capelastegui, Alberto, Zalacain, Rafael, Bilbao, Amaia et al. (2014) Pneumococcal pneumonia: differences according to blood culture results. BMC pulmonary medicine 14: 128

Cilloniz, Catia, Ceccato, Adrian, de la Calle, Cristina et al. (2017) Time to blood culture positivity as a predictor of clinical outcomes and severity in adults with bacteremic pneumococcal pneumonia. PloS one 12(8): e0182436

Dedier J, Singer DE, Chang Y, Moore M, Atlas SJ. Processes of care, illness severity, and outcomes in the management of community-acquired pneumonia at academic hospitals. Archives of Internal Medicine. 2001; 161(17):2099-2104

Falguera M, Ruiz-Gonzalez A, Schoenenberger JA, Touzon C, Gazquez I, Galindo C et al. Prospective, randomised study to compare empirical treatment versus targeted treatment on the basis of the urine antigen results in hospitalised patients with community-acquired pneumonia. Thorax. 2010; 65(2):101-106

Lee JS, Primack BA, Mor MK, Stone RA, Obrosky DS, Yealy DM et al. Processes of care and outcomes for community-acquired pneumonia. American Journal of Medicine. 2011; 124(12):1175-17

Lee, Jonghoo and Song, Jae-Uk (2020) Performance of pneumococcal urinary antigen test in patients with community-onset pneumonia: a propensity score-matching study. The Korean journal of internal medicine 35(3): 630-640

Lidman C, Burman LG, Lagergren A, Ortqvist A. Limited value of routine microbiological diagnostics in patients hospitalized for community-acquired pneumonia. Scandinavian Journal of Infectious Diseases. 2002; 34(12):873-879

Markussen, Dagfinn L, Serigstad, Sondre, Ritz, Christian et al. (2024) Diagnostic Stewardship in Community-Acquired Pneumonia With Syndromic Molecular Testing: A Randomized Clinical Trial. JAMA network open 7(3): e240830

Meehan TP, Fine MJ, Krumholz HM, Scinto JD, Galusha DH, Mockalis JT et al. Quality of care, process, and outcomes in elderly patients with pneumonia. Journal of the American Medical Association. 1997; 278(23):2080-2084

Piso RJ, Iven-Koller D, Koller MT, Bassetti S. The routine use of the urinary pneumococcal antigen test in hospitalised patients with community acquired pneumonia has limited impact for adjustment of antibiotic treatment. Swiss Medical Weekly. 2012; 142

Shen, Ching-Fen; Wang, Shih-Min; Liu, Ching-Chuan (2011) A new urinary antigen test score correlates with severity of pneumococcal pneumonia in children. Journal of the Formosan Medical Association = Taiwan yi zhi 110(10): 613-8

Uematsu H, Hashimoto H, Iwamoto T, Horiguchi H, Yasunaga H. Impact of guideline-concordant microbiological testing on outcomes of pneumonia. International Journal for Quality in Health Care. 2014; 26(1):100-107

van der Eerden MM, Vlaspolder F, de Graaff CS, Groot T, Bronsveld W, Jansen HM et al. Comparison between pathogen directed antibiotic treatment and empirical broad spectrum antibiotic treatment in patients with community acquired pneumonia: a prospective randomised study. Thorax. 2005; 60(8):672-678

Virk A, Strasburg AP, Kies KD, Donadio AD, Mandrekar J, Harmsen WS, Stevens RW, Estes LL, Tande AJ, Challener DW, Osmon DR, Fida M, Vergidis P, Suh GA, Wilson JW, Rajapakse NS, Borah BJ, Dholakia R, Reed KA, Hines LM, … Patel R. (2024). Rapid multiplex PCR panel for pneumonia in hospitalised patients with suspected pneumonia in the USA: a single-centre, open-label, pragmatic, randomised controlled trial. The Lancet. Microbe, 5(12), 100928

1.1.14.2 Economic evidence

National Institute of Health and Care Excellence (NICE), CG191, accessed at: https://www.nice.org.uk/guidance/cg191/evidence/appendix-l-costeffectiveness-analysis-pdf-400830279448

Xie, Xuanqian; Sinclair, Alison; Dendukuri, Nandini (2017) Evaluating the accuracy and economic value of a new test in the absence of a perfect reference test. Research synthesis methods 8(3): 321-332

1.1.11 The committee's discussion and interpretation of the evidence

1.1.11.1. The outcomes that matter most

The committee agreed that the main purpose of this review was to determine whether microbiological tests could reliably inform treatment decisions in people with community acquired pneumonia (CAP) or hospital acquired pneumonia (HAP). Therefore, the key outcomes were those relating to treatment decisions. Choice of antibiotic, change in antibiotic and treatment duration were the most important outcomes on this basis. The committee agreed that a range of surrogate outcomes could be used to support their decision making, so they were also interested in outcomes that indicated severe disease such as need for mechanical ventilation, need for ITU admission and length of hospital stay. The committee were also concerned about antimicrobial resistance, but no evidence on this outcome was available.

1.1.12.2 The quality of the evidence

The existing evidence base for this review consisted of 9 studies: 2 test and treat randomised controlled trials and 7 cohort studies. These provided evidence on blood culture tests, sputum culture tests, and urinary antigen tests. None of the existing evidence was from the UK. The committee recognised that overall there was very little new evidence in this area, with 2 test and treat randomised controlled trials and five prognostic cohort studies matching the criteria in the protocol. The prognostic studies examined blood culture tests and urinary antigen tests, but the data from these studies could not be pooled with data from the previous review because the comparisons were different. The two new RCTs examined PCR tests, which was a new area of evidence.

The committee noted that the PCR tests used a method of sample collection which would not be routinely used in UK hospitals, but that they were generally well conducted trials. They noted that the trials had a clear definition of pneumonia and included an extensive and reliable microbiological lower airway sampling regime that minimised contamination of samples with upper airway pathogens. The committee discussed the importance of understanding the pathogen involved and potential impacts of this on antimicrobial stewardship.

Since only 2 test and treat RCTs were found, the committee agreed that, even though they did not directly address the question, further prognostic cohort studies that looked at outcomes following a microbiological test might provide some useful context. Although these studies did not test treatment decisions based on microbiological tests, they did convey the accuracy of those tests in predicting severe disease, which could in turn be used, alongside the committee's expertise and experience, to make recommendations about treatment decisions. The committee agreed that the five prognostic cohort studies included in the review were at moderate to high risk of bias, due to limitations in the study design, possible selection bias and missing outcome data. They noted that 3 of the 5 studies were conducted in

Spain, and the other 2 in Taiwan and Korea, raising some concerns about the directness of the evidence. Overall, the quality of the prognostic evidence was very low, with most outcomes graded as very low confidence.

The recommendations that were to be updated by this review covered both the adult population and babies, children and young people. It was important for the committee to consider evidence across all age groups Only one cohort study using pneumococcal urinary antigen test (PUAT) provided evidence for babies, children and young people, which was at high risk of bias, conducted in a non-OECD country and had low vaccination rates in the sample population. The committee discussed this evidence and agreed that the evidence was not applicable to the UK context so were not confident to base recommendations on it. The committee instead made recommendations for babies, children and young people by extrapolating from the adult evidence and using their knowledge and experience to make consensus recommendations.

1.1.12.3 Benefits and harms

The committee noted that the review for the current recommendations was of evidence for people who were presenting in secondary care, i.e. they were being admitted to hospital. As a result, they did not amend the 2014 recommendation for people with low-severity CAP as these are less likely to be managed in secondary care and because current practice is to not offer testing to this group. They agreed and amended the recommendation to include the addition of children with non-severe community acquired pneumonia as the 2014 recommendation was for adults only.

The committee discussed the evidence from Markussen (2024) and Virk (2024). Evidence from these test and treat RCTs showed that the committee could have low to moderate confidence in the evidence that people who had a PCR test would be more likely to get pathogen directed treatment, and moderate confidence in the evidence that they would be less likely to be admitted to ICU at 96 hours. The evidence did not show any change in length of hospital stay for people who had pathogen directed treatment or standard treatment, and the study found no difference in mortality, readmission, or admission to ICU within a 30 day time frame. The committee discussed the relevance of the test and treat RCT interventions to the United Kingdom. They were largely in agreement that the BioFire FilmArray assay used in the studies was labour, time and cost intensive and thus may not be feasible to use in secondary care within the UK. They noted that it required laboratory input and therefore would be subject to laboratory waiting times and opening hours and that the test may be difficult to implement in near patient or on unit testing in EDs. On the basis of the lack of evidence and the low confidence in the evidence and the difficulties with rolling out such an intervention in the UK, they agreed not to make a recommendation about PCR testing. However, they were mindful of future research, particularly in terms of the ability of PCR testing to move people quickly onto narrow spectrum antibiotics and the potential impact of this on antimicrobial stewardship. As research is ongoing a research recommendation was not developed in this area.

The committee recognised that the evidence from the prognostic studies demonstrated some correlation between positive blood cultures for *S. Pneumoniae* bacteraemia and negative outcomes such as treatment failure, mortality and need for ITU admission or invasive mechanical ventilation, however the committee could only have low or very low confidence in the findings due to concerns about risk of bias, indirectness and imprecision. Based on their clinical expertise and experience, they agreed that even if the findings were correct, it would not have much impact on treatment decisions for many patients because blood cultures take some time to report and by the time a pathogen is confirmed patients are often nearing the end of their treatment. The time lag for blood cultures and the small number of patients who test positive means they are rarely useful in clinical practice unless the patients require additional treatment, or sepsis or a more complicated pneumonia is suspected, and added a recommendation to reflect this. The committee noted that the previous guideline had recommended both blood and sputum culture, however these recommendations were based on committee consensus rather than on evidence of effectiveness, and that best practice had moved on since that guideline's publication in 2014, therefore these recommendations needed updating. The committee highlighted that blood culture analysis is standard practice already in emergency departments for adults with suspected sepsis and that pathogen isolation has an important role in lab serotyping which informs national vaccination. The committee agreed that for those with moderate or high severity community acquired pneumonia that blood culture analysis should be considered if there are additional clinical indications.

The committee agreed that the prognostic evidence showed that there is no meaningful difference between length of stay in hospital or duration of antibiotic course between adults with a positive or negative urinary antigen test, however they could only have very low confidence in this evidence due to concerns about risk of bias, indirectness and imprecision. In children, a strongly positive urinary antigen test (determined by depth of colour of reagent and time to reaction) did correlate with admission to ITU, oxygen requirement and invasive mechanical ventilation. The committee noted that this evidence was very low confidence and not applicable to the UK. The committee discussed the use of urinary antigen tests in clinical practice and had mixed views on the benefits of using these tests. Some committee members highlighted concerns about the accuracy and appropriateness of such tests, whereas others acknowledged their usefulness. Considering these concerns around the usefulness in practice and the very limited evidence in children the committee agreed not to recommend the use of these tests in children. Overall, the committee agreed that there were circumstances in which urinary antigen tests could be useful in adults for example antibiotic streamlining to choose an antibiotic for high severity patients, which would contribute to reducing antimicrobial resistance. The committee agreed to preserve the consensus recommendation made by the 2014 committee to consider the use of these tests in adults.

1.1.12.4 Cost effectiveness and resource use

There were two existing cost-effectiveness studies for this review question. These included model-based economic evaluation by Xie 2017 in Canada and the model from the previous iteration of the NICE pneumonia guideline 2014. Xie 2017 showed that the addition of a urinary antigen test to a culture had the potential be cost effective. However, there were potentially serious limitations including the study being from the perspective of a single hospital and the baseline outcomes were based on expert opinion.

The model developed for the previous iteration of this guideline assessed multiple tests and found that blood and sputum cultures were the most cost-effective options. However, there were potentially serious limitations associated with this analysis including some of key data inputs, including effectiveness data, sourced from expert opinion.

The committee acknowledged that currently the use of microbiological tests varies and sometimes these tests are used inappropriately. The committee discussed that blood culture results often take too long to impact the treatment pathway, leading the committee to question their value. Some hospitals are starting to reduce the number of people they test. Therefore, given the above, the committee decided not to recommend blood and sputum cultures.

The committee felt that urinary antigen tests were better at informing treatment plans. The committee noted that urinary antigen tests cost around £20 and are likely to be cheaper than other tests, especially those sent to a laboratory. A Canadian study provided limited evidence that using urinary antigen tests alongside cultures resulted in an ICER of £449 per case correctly identified. The committee believed this showed that these tests are potentially cost-effective. The committee noted that urinary antigen tests could be useful in certain situations for example if there is uncertainty with prescribing antibiotics. Without these tests, more people might be prescribed antibiotics unnecessarily or inappropriately, undermining effective antibiotic stewardship.

Urinary antigen tests were recommended in the previous iteration of the NICE guideline on Pneumonia and therefore will not require additional resource to implement. Blood and sputum cultures were also recommended in the previous iteration of the guideline. Therefore, the new recommendation, to only take blood cultures if suspecting sepsis or take a sputum culture if there is a likelihood of getting a good quality sample, will reduce the number of these cultures taken, potentially leading to cost-savings for the NHS. Overall, streamlining the testing process to only using urinary antigen test, where needed, is likely to be cost saving strategy without detrimental impact on patient outcomes.

Similarly, urinary antigen tests are occasionally used in babies and children. With the new recommendation to only take blood cultures if suspecting sepsis or take a sputum culture if there is a likelihood of getting a good quality sample, their use will

decrease, leading to fewer negative outcomes and potential cost savings for the NHS.

1.1.12.5 Other factors the committee took into account

The committee recognised that overall there was a lack of good quality, directly relevant evidence in this area. They emphasised the potential role of microbiological tests in reducing rates of empirical prescribing and support more directed antibiotic therapy. In particular, point of care tests and multiple pathogen panels may help to direct the treatment approach within less than 24 hours. They could also help to safely identify patients who do not require antibiotics, further supporting antimicrobial stewardship. They therefore made a research recommendation to determine which microbiological tests can safely reduce antibiotic prescribing in people with suspected pneumonia.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.4.5 to 1.4.7.

Appendices

Appendix A – Review protocol

What are the most effective and cost-effective microbiological tests or combination of tests at presentation in secondary care to inform treatment decisions in people with suspected community-acquired pneumonia or suspected hospital-acquired pneumonia?

Review title	What are the most effective and cost-effective microbiological tests or combination of tests at presentation in secondary care to inform treatment decisions in people with suspected community-acquired pneumonia or suspected hospital-acquired pneumonia?
Review question	What are the most effective and cost-effective microbiological tests or combination of tests at presentation in secondary care to inform treatment decisions in people with suspected community-acquired pneumonia or suspected hospital-acquired pneumonia?
Objective	To establish the effectiveness and prognostic accuracy of various microbiological tests (including blood culture, sputum culture, urinary pneumococcal antigen, urinary legionella antigen) compared to clinical assessment alone to inform treatment decisions (including no treatment) for patients with suspected CAP or HAP, at presentation in secondary care.
Searches	**Overall approach** The searches will comprise the following elements: • a combined search for cost effectiveness evidence covering all review questions in this guideline. • a combined search for systematic reviews covering all review questions in this guideline. • searches for effectiveness evidence specific to this review question, which will be further divided into a search relating to adults and a search covering children and young people. **Searches for cost effectiveness evidence** A combined search will be undertaken to cover the cost effectiveness aspects of all the review questions in a single search.

	The following databases will be searched for the cost effectiveness evidence: • Econlit via Ovid • Embase via Ovid • International HTA database via INAHTA website • MEDLINE ALL via Ovid The sensitive version of the validated NICE cost utility filter will be applied to the MEDLINE and Embase search strategies (Hubbard et al., 2022 [doi: 10.1186/s12874-022-01796-2]). Searches for cost effectiveness evidence will be limited to 2014-current (the searches for NICE guideline CG191 were completed in March 2014). The MEDLINE and Embase searches will be limited to evidence from Organisation for Economic Co-operation and Development (OECD) member states using the validated NICE filter (Ayiku et al., 2021 [doi: 10.5195/jmla.2021.1224]). **Effectiveness evidence: combined search for systematic reviews** The search for systematic reviews relating to all review questions in this guideline will cover reviews published since the searches for NICE guideline CG191 were completed in March 2014. The sources for this will be: • Cochrane Database of Systematic Reviews (CDSR) via Wiley • Epistemonikos via https://www.epistemonikos.org/ This is the standard NICE practice agreed by the Guidelines Methods Group in September 2022 for identifying systematic reviews for routine guideline searches. **Effectiveness evidence: searches specific to this review question** The searches for effectiveness evidence specific to this review question will use the following databases: • Cochrane Central Register of Controlled Trials (CENTRAL) via Wiley • Embase via Ovid • MEDLINE ALL via Ovid

	The principal search strategy will be developed in MEDLINE and then adapted, as appropriate, for use in the other sources listed, taking into account their size, search functionality and subject coverage. To ensure potentially relevant records are not missed the following will be checked as required: • The reference lists of any appropriate studies • Later citations of any key trials, reviews, studies or protocols. The seed references for these actions will be identified from the search for systematic reviews, the scoping searches for this guideline, or the evidence reviews for previous NICE guidelines. The guideline committee or other stakeholders could also be asked if they are aware of any other potentially relevant studies that could be considered. The searches will be split into a strategy covering adults and a separate strategy covering children and young people. The searches relating to adults will be conducted from March 2014. The searches relating to children will not have a date limit. Both searches will apply appropriate validated study filters for prognostic studies. The MEDLINE and Embase searches will be limited to OECD member states using the validated NICE filter. **Managing all search results** Database functionality will be used, where available, to exclude from all searches: • Animal studies • Conference abstracts and posters • Editorials, letters, news items and commentaries • Registry entries for ongoing clinical trials or those that contain no results • Theses and dissertations • Papers not published in the English language With the agreement of the guideline committee, the searches will be re-run 6-8 weeks before final submission of the review and further studies retrieved for inclusion. The information services team at NICE will quality assure the principal search strategy and peer review the other

	strategies. Any revisions or additional steps will be agreed by the review team before being implemented. The full search strategies for all databases will be published in the final review.
Condition or domain being studied	Community acquired pneumonia. Hospital acquired pneumonia.
Population	**Inclusion:** Babies over 28 days (corrected gestational age), children, young people (age <18 years) and adults (≥18 years) with pneumonia (community or hospital acquired) requiring management in hospital. • CAP is defined as pneumonia that is acquired outside hospital • HAP is defined as pneumonia that occurs 48 hours or more after admission to hospital and is not incubating at hospital admission, or within 10 days of a previous hospital admission for a different problem. Note: studies that include a broader population (e.g. sepsis) will be included if: (a) they give results stratified for pneumonia; or (b) ≥ 75% patients have pneumonia. **Exclusion:** • Babies up to and including 28 days (corrected gestational age). • People with COVID-19 pneumonia. • People who acquire pneumonia while intubated (ventilator-associated pneumonia). • People who are severely immune-compromised (have a primary immune deficiency or secondary immune deficiency related to HIV infection, or severe drug or systemic disease-induced immunosuppression, for example, people who have taken immunosuppressant cancer therapy or undergone organ transplantation).

	• People in whom pneumonia is an expected terminal event. • People with non-pneumonic infective exacerbations of bronchiectasis. • People with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • People with pneumonia associated with cystic fibrosis. • People with aspiration pneumonia as a result of inhaling a large bolus of gastric contents.
Intervention	Microbiological tests, alone or in combination: - blood culture - sputum culture - urinary pneumococcal antigen - urinary legionella antigen - molecular testing of sputum or throat swab: o Single-plex o Multi-plex Note that due to the difficulty with obtaining sputum samples in children under 5, throat swabs or nasal swabs are more appropriate for this age group. Invasive sampling techniques (e.g. bronchoalveolar lavage and protected brush sampling) will not be considered as they are only applicable to a small proportion of the population.
Comparator	Usual care / clinical assessment alone
Types of study to be included	Systematic reviews of RCTs and prognostic cohort studies test and treat RCTs Prognostic cohort studies We will use a stepwise approach, so if insufficient RCTs or prospective studies (e.g. <5 good quality, directly relevant papers) then we will look at retrospective; but retrospective will be excluded if we identify enough RCTs or prospective studies.

Other exclusion criteria	We will not include studies that only report the proportion of tests that gave a positive result – these studies need to link the test results with change in management.
Context	The various microbial causes of community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) are each sensitive or resistant to different antibiotics. Unfortunately clinical, chest X-ray (CXR) and laboratory features do not allow accurate identification of the microbial cause in an individual patient. Empirical antibiotic therapy is usually commenced at patient presentation based on knowledge of likely pathogens. Targeting the correct antibiotic to the microbial cause in an individual patient is desirable. Traditional practice has been to send specimens (for example, of blood and or sputum) from each patient to the microbiology laboratory to try to identify the microbial cause in that patient and so refine the empirical antibiotic therapy. While a specific microbial cause is sometimes identified by this means, in the majority of cases no cause is found. The tests most commonly used are blood culture and sputum culture. Two urine antigen detection tests are also available in most hospitals. However, various factors can limit the clinical usefulness of these microbiological tests, and they have an associated cost. It is important to know which tests, or combination of tests, are clinically and cost-effective in managing treatment decisions in patients with CAP or HAP.
Primary outcomes (critical outcomes)	• Mortality within 30 days • Change in antibiotic and choice of antibiotic (broad or narrow spectrum) • Treatment duration • ICU admission • Need for invasive ventilation • Length of hospital stay • Length of ICU stay • Hospital re-admission within 30 days For test and treat RCTs, we will report outcome data for intervention and control groups.

	For prospective observational studies, we will use HRs, ORs and RRs. Where reported we will include • Sens/spec • LR+/- • AUC. Sens/spec will be converted to LR
Secondary outcomes (important outcomes)	• HRQoL (measured using validated tools such as the EQ5D or SF-36; or using condition-specific measures of QoL such as the CAP Symptom Questionnaire or the St George's Respiratory Questionnaire) • Adverse events e.g. hospital acquired infection, treatment side effects, C. diff, antimicrobial resistance, hospital infection outbreaks
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. Any disagreements will be resolved by discussion with other members of the technical review team. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For SRs, the ROBIS (Risk of Bias in Systematic Reviews) checklist will be used. For RCTs, the Cochrane risk of bias (RoB) 2 tool will be used.

	For observational studies, the Cochrane ROBINS-I tool will be the preferred tool. The CASP cohort study checklist will be used if ROBINS-I is not appropriate. For prospective studies, we will use the QUIPS checklist.
Strategy for data synthesis	Where possible, meta-analyses of outcome data will be conducted for all comparators that are reported by more than one study, with reference to the Cochrane Handbook for Systematic Reviews of Interventions. Where data can be disambiguated it will be separated into the subgroups identified in section 17 (below). Continuous outcomes will be analysed as mean differences, unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all comparators, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions is met: Significant between study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$. In any meta-analyses where some (but not all) of the data comes from studies at high risk of bias, a sensitivity analysis will be conducted, excluding those studies from the analysis. Results from both the full and restricted meta-analyses will be reported. Similarly, in any meta-analyses where some (but not all) of the data comes from indirect studies, a sensitivity analysis will be conducted, excluding those studies from the analysis.

	GRADE will be used to assess the quality of the outcomes. All outcomes in this review will be rated as high quality initially and downgraded from this point. Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically (visually) assess the potential for publication bias. Minimally important differences (MIDs) will be discussed with the committee and if established MIDs are not identified, default MIDs will be used. These are 0.80 and 1.25 for dichotomous outcomes, and 0.5 times the control group SD for continuous outcomes.
Analysis of sub-groups	The following groups will be considered separately if data are available: • CAP and HAP • Age: 0-1; 1-5; 5-18; Adults • CAP severity measured by PSI or CURB-65 • Antibiotic therapy before admission
Type and method of review	☒ Intervention ☐ Diagnostic ☒ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)

AUC=area under the curve; CAP=community acquired pneumonia; CXR=chest X-ray; GRADE=Grading of Recommendations Assessment, Development and Evaluation; EQ-5D=EuroQol health related quality of life (5 domains); HAP=hospital acquired pneumonia; HRQoL=health related quality of life; ICU=intensive care unit; HR=hazard ratio; MID=minimally important difference; NHS=National health service; NICE=National Institute for Health and Care Excellence; N/A=Not applicable; OR=odds ratio; PHQ-9=Patient health questionnaire-9; PROSPERO=International prospective register of systematic reviews; RCT=randomised controlled trial; RoB=risk of bias; ROBINS-I=risk of bias In non-randomized studies of interventions; ROBIS=risk of bias in systematic reviews; RR=risk ratio; SD=standard deviation SF-12=12-item short form survey

Appendix B – Literature search strategies

Background and development

Overall approach

Each evidence review for this guideline has a search conducted in three parts:

- Part 1: Systematic review searches

A single search for all systematic reviews relating to pneumonia published from 2014-current was done separately in November 2023 and re-run in October 2024. The results were screened for relevance to all the review questions. The potentially relevant results from this search were also used to create the seed references for reference list checking and forward citation searching for the effectiveness and prognostic evidence searches.

- Part 2: Effectiveness and prognostic evidence searches

This search was developed separately and tailored to each evidence review. The searches for effectiveness and prognostic evidence (Part 2) were run on 13 March 2024. For this review, it was further divided into two parts: 2A (covering adults since March 2014); and 2B (children and young people with no date limits). The results of these searches were then combined and deduplicated for screening.

- Part 3: Cost effectiveness searches

A single search covering the cost effectiveness elements of all review questions was done separately in November 2023 and re-run in October 2024. This was a top-level search for all cost utility studies published from 2014-current.

Search design and peer review

A NICE Senior Information Specialist (SIS) conducted the literature searches for each part.

This search report is based on the requirements of the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (for further details see: Rethlefsen M et al. PRISMA-S. *Systematic Reviews*, 10(1), 39).

The MEDLINE strategies below were quality assured (QA) by a trained NICE SIS. All translated search strategies were peer reviewed by another SIS to ensure their accuracy. Both procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

Review management

All search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess 'low-probability' matches. All decisions made for the review can be accessed via the deduplication history.

Search limits, restrictions and filters

Formats

Limits were applied in adherence to standard NICE practice (as set out in the Identifying the evidence chapter of the manual) and the eligibility criteria listed in the review protocol to exclude:

- Animal studies
- Case reports
- Conference abstracts and posters
- Editorials, letters, news items and commentaries
- References not published in the English language
- Registry entries for ongoing clinical trials or those that contain no results
- Theses and dissertations.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from:

> Dickersin K, Scherer R & Lefebvre C. (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. *BMJ*, 309(6964), 1286.

OECD

For the Effectiveness (Part 2) and Cost Effectiveness (Part 3) searches, the validated NICE OECD filters were used in MEDLINE and Embase to remove records exclusively set in countries that are not members of the Organisation for Economic Co-operation and Development (OECD), in line with the search protocol. The filters were used without amendment. The filters are not available for the other databases used. The OECD filters were not applied to the Systematic Review (Part 1) searches.

> Ayiku L et al. (2021) The NICE OECD countries' geographic search filters: Part 2 - Validation of the MEDLINE and Embase (Ovid) filters. *Journal of the Medical Library Association*, 109(4), 583–589.

Date limits

A date limit of 2014-current was applied to the Systematic Review (Part 1) and Cost Effectiveness (Part 3) searches. This date limit was used because the searches for

NICE CG191 Pneumonia in adults: diagnosis and management (published in December 2014) were last run on 17 March 2014.

The Effectiveness searches (Part 2) were limited as follows:

- Part 2A: 1 March 2014 onwards as this was an update of CG191.
- Part 2B: no date limit as this population had not been considered previously.

Study-type filters

The Systematic Review (Part 1) searches had no filters, as the content for CDSR and Epistemonikos is pre-filtered.

The Effectiveness searches for Part 2 used RCT and prognostic study filters, in line with the protocol.

The standard RCT filters in use at NICE were applied. The MEDLINE RCT filter was McMaster Therapy – Medline – "best balance of sensitivity and specificity" version. The standard NICE modifications were used: the MeSH heading randomized controlled trial/ (equivalent to randomized controlled trial.pt) was exploded to capture newer, narrower terms; and the free-text term randomized.mp was changed to randomi?ed.mp. to capture both UK and US spellings.

> Haynes RB et al. (2005) Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey. *BMJ*, 330, 1179-1183.

The Embase RCT filter was McMaster Therapy – Embase "best balance of sensitivity and specificity" version.

> Wong SSL et al. (2006) Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. *Journal of the Medical Library Association*, 94(1), 41-47.

The Prognostic Study Filter was the current version of the NGA filter that was used in the CG191 searches (last updated 17/11/21). The filter was amended with the addition of MeSH and Emtree terms for Prognosis, which testing showed would increase recall of potentially relevant papers, although it is acknowledged that this also affected the precision.

Cost effectiveness searches

In line with the protocol, the validated NICE Cost Utility Filter was used in the MEDLINE and Embase searches for Cost Effectiveness (Part 3). The sensitive version of the filter was selected and it was used without amendment. Subject coverage in the Econlit, International HTA Database and NHS EED databases is already pre-specified and so it is not appropriate to apply filters in them.

> Hubbard W et al. (2022) Development and validation of paired MEDLINE and Embase search filters for cost-utility studies. *BMC Medical Research Methodology*, 22(1), 310.

Key decisions

Part 1: Systematic review searches

This search was conducted according to the standard NICE practice since the "Proposal to limit systematic review (SR) searching for routine guideline searches" was accepted by the NICE Guideline Methods Group (GMG) in September 2022. This process means that only sources which aggregate systematic reviews are searched in addition to the Cochrane Database of Systematic Reviews. The methods used to aggregate reviews for Epistemonikos are sufficiently sensitive with higher precision (Rada et al., 2020) compared to using standard Boolean search filters in general medical databases (Lee et al., 2012). Testing during scoping showed that other aggregators of systematic reviews, such as the Campbell Collaboration, Dopher and Health Evidence, would not be relevant for inclusion in this protocol.

Lee E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. *BMC Medical Research Methodology,* 12(1), 51.

Rada G et al. (2020) Epistemonikos: a comprehensive database of systematic reviews for health decision-making. *BMC Medical Research Methodology*, 20, 286.

Parts 1-3: Pneumonia terms

The same set of pneumonia terms was developed in November 2023 to use in all evidence reviews for this guideline. These terms aimed to cover all the included populations named in the final scope (section 3.1), namely babies over 28 days (corrected gestational age), children, young people and adults with suspected or diagnosed community-acquired or hospital acquired pneumonia.

A set containing 183 items was created to test the comprehensiveness of the searches. The 183 records were derived from the papers included in CG191 and the papers included in the 10 most recent Cochrane reviews about pneumonia.

The search terms built on the search strategies developed for NICE CG191 Pneumonia in adults and two antibiotic prescribing guidelines (NG138 and NG139).

The CG191 searches had a line to NOT out the MeSH term "pneumonia, ventilator-associated". This was not retained in the search as it was inadvertently excluding relevant papers that discussed several types of pneumonia (e.g. see PMIDs 29722052 or 32822880 or 28655326 or 34823043).

The CG191 searches truncated the free text to pneumoni* but this was amended following clinical advice that pneumonia is a form of pneumonitis but not all pneumonitis is pneumonia.

The CG191 searches had an additional line describing chest infection. It was not necessary to retain this line in order to retrieve any of the 183 items in the test set and so it was removed, which reduced the population search by around 41,000 results in MEDLINE.

The previous strategies could not be used directly because of changes to Medical Subject Headings (MeSH) since 2019. Using the previous searches would now retrieve all MEDLINE results about COVID-19, as well as pneumonia. It is now

necessary to choose individual MeSH headings from the hierarchy. The choice of headings was made in conjunction with the technical team in the scoping searches in October 2023. Headings for Aspiration, Lipid, Enzootic and Swine Pneumonia, as well as Pneumocystis and COVID-19 were not included. This approach reduced the number of results with just the population terms from 340,000 with the CG191 approach to 124,000. None of the test set were lost by adopting this approach.

Seven options were then tested to optimise the precision of the pneumonia free-text terms. The options tested the feasibility of excluding free-text terms for aspects known to be out of scope (such as COVID-19 or ventilator-associated pneumonia). None of the options made a sufficient difference to the volume to justify making the strategies much more complicated and risk missing relevant papers (the most plausible option only reduced the entire pneumonia literature from 227,500 to 225,900 results). The option to add further free text to define the relevant types of pneumonia (such as bacterial pneumonia) was rejected as it risked missing relevant papers because some abstracts just referred to treating pneumonia, without specifying which type or subtype it was.

At the committee meeting GCOMM1 on 20 December 2023 feedback was received from the committee that rickettsial and cryptogenic organizing pneumonia were not relevant to the UK context and could safely be removed from the search strategies. These terms feature in the Part 1 systematic review and Part 3 cost effectiveness searches as these were completed before the meeting (and were retained in the re-runs for consistency).

The same approach to subject headings was applied in Embase, although the COVID-19 headings are not part of the pneumonia hierarchy in Emtree. The following headings from the pneumonia hierarchy were not chosen: Acute chest syndrome, Acute lupus pneumonitis, Allergic pneumonitis, Aspiration pneumonia, Chemical pneumonitis, Enzootic pneumonia, Eosinophilic pneumonia, Loeffler pneumonia, Experimental pneumonia, Lung infiltrate, Pneumonic effusion, Radiation pneumonia, Parasitic pneumonia, Pneumocystis pneumonia, Pulmonary candidiasis, Pulmonary toxoplasmosis, Legionnaire disease, Pulmonary actinomycosis, Ventilator associated pneumonia, Ventilator associated bacterial pneumonia, Checkpoint inhibitor pneumonitis, and Severe acute respiratory syndrome. Searches after 20/12/23 also excluded Rickettsial pneumonia and Bronchiolitis obliterans organizing pneumonia.

The same free-text terms developed initially in MEDLINE were used in Embase.

The re-run searches were identical to the main search strategies. Re-runs are date limited to the first day of the month in which the main search was run to the current date. In MEDLINE the create date (.dt) and entry date (.ed) fields were used. In Embase the date created (.dc) field was used. In CENTRAL, the post-search filter "Date added to CENTRAL trials database" was used.

Part 2: Effectiveness and prognostic evidence searches

The strategies are in the structure:

Part 2A: Pneumonia AND Microbiological Tests AND Treatment Decisions AND (RCTs or Prognosis) AND Limits AND 2014-Current

Part 2B: Pneumonia AND Microbiological Tests AND Treatment Decisions AND (Children OR Young People) AND (RCTs or Prognosis) AND Limits

The search results for Part 2A and 2B were screened in one single EPPI-Reviewer file. There were separate searches because adults had already been covered in CG191. The terms for pneumonia, the interventions and study-type filters were identical in both searches. The date limits were adjusted, with Part 2A limited to March 2014 onwards and Part 2B having no date limits. The search terms for children and young people in Part 2B were adapted from a previous search for this guideline (Corticosteroids for treating pneumonia in children search Part 2C). Using a single EPPI file reduced the number of duplicates.

The search covers the interventions listed in the protocol. General terms for microbiological tests were also included to cover records comparing different types of test.

The search includes a set of terms for settings, treatment decisions and relevant outcomes. A test set of 23 papers, including 21 for adults and 2 for children, was created from results of the search for systematic reviews, the scoping searches and the included papers in CG191. This set was used to distinguish relevant papers from those about diagnostic accuracy, diagnostic performance and the sensitivity or specificity of the test.

The Emtree terms for the microbiological tests were all focussed. This reduced the test search from 5624 to 3143. A sample of the papers that would be missed was reviewed and none were relevant to this protocol.

Part 1: Systematic review searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Database of Systematic Reviews (CDSR)	20/11/2023	Wiley	Cochrane Database of Systematic Reviews Issue 11 of 12, November 2023	177
Epistemonikos	20/11/2023	Epistemonikos	Version available on 20/11/23	2096

Re-run results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Database of Systematic Reviews (CDSR)	15/10/2024	Wiley	Cochrane Database of Systematic Reviews Issue 10 of 12, October 2024	8

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Epistemonikos	15/10/2024	Epistemonikos	Version available on 15/10/2024	2571

Search strategy history

Database name: Cochrane Database of Systematic Reviews (CDSR)

Searches
#1 [mh ^pneumonia] or [mh ^bronchopneumonia] or [mh ^pleuropneumonia] or [mh ^"pneumonia, bacterial"] or [mh ^"chlamydial pneumonia"] or [mh ^"pneumonia, mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, rickettsial"] or [mh ^"pneumonia, staphylococcal"] or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"cryptogenic organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 5252
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15137
#3 #1 or #2 16754
#4 #1 or #2 in Cochrane Reviews 244
#5 #1 or #2 with Cochrane Library publication date Between Jan 2014 and Nov 2023, in Cochrane Reviews 177
Note: in the re-run Line #5 was changed to #1 or #2 with Cochrane Library publication date Between Nov 2023 and Oct 2024, in Cochrane Reviews.

Database name: Epistemonikos

Searches
These are the lines as they were input into the interface for the re-run:
1 title:(bronchopneumonia* OR pleuropneumonia* OR broncho-pneumonia OR pleuro-pneumonia or broncho-pneumonias OR pleuro-pneumonias OR "broncho pneumonia" OR "pleuro pneumonia" or "broncho pneumonias" OR "pleuro pneumonias")
2 abstract:(bronchopneumonia* OR pleuropneumonia* OR broncho-pneumonia OR pleuro-pneumonia or broncho-pneumonias OR pleuro-pneumonias OR "broncho pneumonia" OR "pleuro pneumonia" or "broncho pneumonias" OR "pleuro pneumonias")
3 title:(pneumonia OR pneumonias)
4 abstract:((pneumonia OR pneumonias) AND (HAP OR nosocomial* OR crossinfect* OR cross-infection OR cross-infected OR cross-infecting OR "cross infection" OR "cross infected" OR "cross infecting" or hospitalised* or hospitalized* or hospitalisation* or hospitalization*))
5 abstract:((pneumonia OR pneumonias) AND ("healthcare acquire" OR "healthcare acquired" OR "healthcare acquiring" OR "healthcare onset" OR "healthcare associate" OR "healthcare associated" OR "healthcare associating"))
6 abstract:((pneumonia OR pneumonias) AND ("health care acquire" OR "health care acquired" OR "health care acquiring" OR "health care onset" OR "health care associate" OR "health care associated" OR "health care associating"))
7 abstract:((pneumonia OR pneumonias) AND ("hospital acquire" OR "hospital acquired" OR "hospital acquiring" OR "hospital onset" OR "hospital associate" OR "hospital associated" OR "hospital associating"))

Searches
8 abstract:((pneumonia OR pneumonias) AND ("inpatient acquire" OR "inpatient acquired" OR "inpatient acquiring" OR "inpatient onset" OR "inpatient associate" OR "inpatient associated" OR "inpatient associating"))
9 abstract:((pneumonia OR pneumonias) AND (healthcare-acquire OR healthcare-acquired OR healthcare-acquiring OR healthcare-onset OR healthcare-associate OR healthcare-associated OR healthcare-associating))
10 abstract:((pneumonia OR pneumonias) AND (health-care-acquire OR health-care-acquired OR health-care-acquiring OR health-care-onset OR health-care-associate OR health-care-associated OR health-care-associating))
11 abstract:((pneumonia OR pneumonias) AND (hospital-acquire OR hospital-acquired OR hospital-acquiring OR hospital-onset OR hospital-associate OR hospital-associated OR hospital-associating))
12 abstract:((pneumonia OR pneumonias) AND (inpatient-acquire OR inpatient-acquired OR inpatient-acquiring OR inpatient-onset OR inpatient-associate OR inpatient-associated OR inpatient-associating))
13 abstract:((pneumonia OR pneumonias) AND (CAP OR community* OR communities* OR outpatient* OR nonhospital* OR "non hospital" OR non-hospital OR "non hospitalised" OR non-hospitalised OR "non hospitalized" OR non-hospitalized OR "non hospitalisation" OR non-hospitalisation OR "non hospitalization" OR non-hospitalization))
14 abstract:((pneumonia OR pneumonias) AND (bacterial* OR chlamydial* OR mycoplasma* OR pneumococcal* OR rickettsial* OR staphylococcal* OR staphylococcus* OR necrotiz* OR necrotis* OR viral* OR organizing* OR organising* OR cryptogenic* OR bilateral* OR granulomatous* OR infectious* OR interstitial* OR neonatal* OR obstructive* OR lobar* OR escherichia* OR haemophilus* OR hemophilus* OR influenzae* OR nocardiosis* OR streptococcus* OR streptococcal*))
This is the final search as formatted by Epistemonikos:
title:((bronchopneumonia* OR pleuropneumonia* OR broncho-pneumonia OR pleuro-pneumonia OR broncho-pneumonias OR pleuro-pneumonias OR "broncho pneumonia" OR "pleuro pneumonia" OR "broncho pneumonias" OR "pleuro pneumonias")) OR abstract:((bronchopneumonia* OR pleuropneumonia* OR broncho-pneumonia OR pleuro-pneumonia OR broncho-pneumonias OR pleuro-pneumonias OR "broncho pneumonia" OR "pleuro pneumonia" OR "broncho pneumonias" OR "pleuro pneumonias")) OR title:((pneumonia OR pneumonias)) OR abstract:(((pneumonia OR pneumonias) AND (HAP OR nosocomial* OR crossinfect* OR cross-infection OR cross-infected OR cross-infecting OR "cross infection" OR "cross infected" OR "cross infecting" OR hospitalised* OR hospitalized* OR hospitalisation* OR hospitalization*))) OR abstract:(((pneumonia OR pneumonias) AND ("healthcare acquire" OR "healthcare acquired" OR "healthcare acquiring" OR "healthcare onset" OR "healthcare associate" OR "healthcare associated" OR "healthcare associating"))) OR abstract:(((pneumonia OR pneumonias) AND ("health care acquire" OR "health care acquired" OR "health care acquiring" OR "health care onset" OR "health care associate" OR "health care associated" OR "health care associating"))) OR abstract:(((pneumonia OR pneumonias) AND ("hospital acquire" OR "hospital acquired" OR "hospital acquiring" OR "hospital onset" OR "hospital associate" OR "hospital associated" OR "hospital associating"))) OR abstract:(((pneumonia OR pneumonias) AND ("inpatient acquire" OR "inpatient acquired" OR "inpatient acquiring" OR "inpatient onset" OR "inpatient associate" OR "inpatient associated" OR "inpatient associating"))) OR abstract:(((pneumonia OR pneumonias) AND (healthcare-acquire OR healthcare-acquired OR healthcare-acquiring OR healthcare-onset OR healthcare-associate OR healthcare-associated OR healthcare-associating))) OR abstract:(((pneumonia OR pneumonias) AND (health-care-acquire OR health-care-acquired OR health-care-acquiring OR health-care-onset OR health-care-associate OR health-care-associated OR health-care-associating))) OR abstract:(((pneumonia OR pneumonias) AND (hospital-acquire OR hospital-acquired OR hospital-acquiring OR hospital-onset OR hospital-associate OR hospital-associated OR

Searches
hospital-associating))) OR abstract:(((pneumonia OR pneumonias) AND (inpatient-acquire OR inpatient-acquired OR inpatient-acquiring OR inpatient-onset OR inpatient-associate OR inpatient-associated OR inpatient-associating))) OR abstract:(((pneumonia OR pneumonias) AND (CAP OR community* OR communities* OR outpatient* OR nonhospital* OR "non hospital" OR non-hospital OR "non hospitalised" OR non-hospitalised OR "non hospitalized" OR non-hospitalized OR "non hospitalisation" OR non-hospitalisation OR "non hospitalization" OR non-hospitalization))) OR abstract:(((pneumonia OR pneumonias) AND (bacterial* OR chlamydial* OR mycoplasma* OR pneumococcal* OR rickettsial* OR staphylococcal* OR staphylococcus* OR necrotiz* OR necrotis* OR viral* OR organizing* OR organising* OR cryptogenic* OR bilateral* OR granulomatous* OR infectious* OR interstitial* OR neonatal* OR obstructive* OR lobar* OR escherichia* OR haemophilus* OR hemophilus* OR influenzae* OR nocardiosis* OR streptococcus* OR streptococcal*))) **Results:** Total: 48055 Apply Publication Year limits of 2014-2024: 30820 Download 1: Apply Publication type - Systematic Review: 2307 Download 2: Apply Publication type - Broad Synthesis: 223 Download 3: Apply Publication type - Structured Summary: 41 **Note:** The re-run search covered the whole timespan 2014-2024 as the phrases in the free text were updated to use a version with a hyphen and to spell out the words rather than truncating them. The main search had used Publication Year limits of 2014-2023.

Part 2A: Effectiveness and prognostic evidence searches (adults)

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	13/03/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 2 of 12, February 2024	411
Embase	13/03/2024	Ovid	Embase 1974 to 2024 March 12	3178
MEDLINE ALL	13/03/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to March 12, 2024	2433

Additional search techniques

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	12/03/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-03-09	93
Reference list checking	12/03/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-03-09	85
Contact with experts post search	19/12/24	N/A	N/A	1

Search strategy history

Database name: Cochrane Central Register of Controlled Trials (CENTRAL)

Searches	
#1	[mh ^pneumonia] or [mh ^bronchopneumonia] or [mh ^pleuropneumonia] or [mh ^"pneumonia, bacterial"] or [mh ^"chlamydial pneumonia"] or [mh ^"pneumonia, mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, staphylococcal"] or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 4399
#2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15670
#3	#1 or #2 16911
#4	[mh ^"Microbiological Techniques"] 58
#5	(microbiolog* NEAR/2 (test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or sample* or test* or swab* or culture* or screen* or smear* or specimen* or exam* or analys*)):ti,ab 1775
#6	[mh ^"Blood Culture"] 44
#7	((blood* or serolog*) NEAR/2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys*)):ti,ab 58281
#8	((sputum* or mucus* or phlegm* or saliva* or secretion* or oropharyn* or nasopharyn* or nasal* or nose* or pharynx* or pharyngeal* or throat* or trachea* or discharge*) NEAR/2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or aspirat* or antigen* or exam* or analys*)):ti,ab 11287
#9	[mh ^urinalysis] 336
#10	(urinalys* or UAT):ti,ab 3478
#11	(urin* NEAR/3 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys* or legionella* or pneumococc*)):ti,ab 17220
#12	[mh ^"antigens, bacterial"] 516
#13	gram stain*:ti,ab 566
#14	(bacteria* NEAR/2 antigen*):ti,ab 65
#15	[mh ^"Molecular Diagnostic Techniques"] 125

Searches
#16 [mh "Bacterial Typing Techniques"] 338
#17 [mh ^"Bacterial Load"] 488
#18 [mh ^"Viral Load"] 3363
#19 [mh ^"Nucleic Acid Amplification Techniques"] 74
#20 [mh "Polymerase Chain Reaction"] 2834
#21 (molecular* NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)):ti,ab 1491
#22 ((bacteria* or bacterium* or virus* or viral*) NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)):ti,ab 2813
#23 ((bacteria* or bacterium* or virus* or viral*) NEAR/1 (load* or burden*)):ti,ab 7511
#24 ((singleplex* or (single NEXT plex*) or multiplex* or (multi NEXT plex*)) NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or molecular*)):ti,ab 835
#25 (((Polymerase Chain NEXT Reaction*) or PCR) NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or singleplex* or (single NEXT plex*) or multiplex* or (multi NEXT plex*) or realtime* or (real NEXT time*))):ti,ab 6366
#26 (NAAT or NAATs or LAMP):ti,ab 2316
#27 (((Nucleic NEXT Acid*) or DNA or RNA or "loop mediated") NEAR/1 (amplification* or amplify* or amplifies*)):ti,ab 298
#28 (Filmarray* or (Film NEXT array*) or Unyvero* or "Fast Track Diagnostics respiratory panel"):ti,ab 84
#29 {or #4-#28} 105370
#30 #3 and #29 2367
#31 [mh ^"Respiratory Care Units"] or [mh ^"Respiratory Therapy Department, Hospital"] or [mh "Respiratory therapy"] 12054
#32 [mh ^hospitalization] or [mh ^hospitals] or [mh ^"secondary care"]9260
#33 [mh ^"Emergency Service, Hospital"] or [mh ^"Emergency Treatment"] or [mh ^"Emergency Medical Services"] or [mh "Emergency Medicine"] or [mh ^"Intensive Care Units"] 9512
#34 [mh ^"critical pathways"] or [mh ^"Critical Care"] 2960
#35 [mh ^"Referral and Consultation"] or [mh ^Triage] or [mh ^"patient transfer"] or [mh ^"Patient Handoff"] or [mh ^Gatekeeping] 3506
#36 [mh ^"Clinical Decision-Making"] or [mh ^"Practice Patterns, Physicians'"] 2656
#37 [mh ^"Patient acuity"] or [mh ^"Patient Discharge"] or [mh ^"Patient Readmission"] or [mh ^Retreatment] 5259
#38 [mh ^"Treatment Failure"] or [mh ^"Treatment Outcome"] 193930
#39 [mh mortality] 18860
#40 [mh ^"Drug Administration Schedule"] or [mh ^"Duration of Therapy"] or [mh ^"Episode of Care"] or [mh ^"Length of Stay"] 37835
#41 [mh ^"Inappropriate prescribing"] 279
#42 [mh ^"anti-infective agents"] or [mh "anti-bacterial agents"] or [mh "beta Lactam Antibiotics"] or [mh "Antimicrobial Stewardship"] 19450
#43 [mh ^"Infection Control"] or [mh ^"Cross Infection"] 2175
#44 [mh ^Oseltamivir] or [mh ^"Antiviral Agents"] 5806
#45 [mh ^"risk assessment"] or [mh ^"risk management"] 13651

Searches
#46 (hospitaliz* or hospitalis* or rehospitalis* or rehospitaliz*):ti,ab 61219
#47 ((patient* or inpatient*) NEAR/3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or rebound* or revisit* or declin* or worsen* or remission* or deteriorat* or escalat* or deescalat* or acuity* or triage* or triaging* or morbidit* or handover* or handoff* or (hand NEXT over*) or (hand NEXT off*))):ti,ab 54825
#48 ((hospital* or ICU or (intensive NEXT care*) or (intensive NEXT treatment*) or ITU or (high NEXT dependency*) or HDU or (critical NEXT care*) or "A&E" or (secondary NEXT care*) or (respiratory NEXT care*) or (accident near/1 emergenc*)) NEAR/3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)):ti,ab 61099
#49 ((specialist* or specialized* or specialised* or emergenc* or secondary*) NEAR/2 (care* or service* or facility* or facilities* or ward or wards or unit or units or department* or clinic or clinics) NEAR/3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)):ti,ab2908
#50 ((invasive* or artificial*) NEAR/3 (respirat* or ventilat*)):ti,ab 4940
#51 ((discharg* or referral* or referred*) NEAR/3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or interval* or schedul* or period* or threshold*)):ti,ab 9978
#52 (hospital* NEAR/3 ((stay* or episod*) NEAR/3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))):ti,ab 22448
#53 ("length of stay" or "episode of care"):ti,ab 13960
#54 ((therap* or intervention* or treatment*) NEAR/3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or (step* NEXT up) or (step* NEXT down) or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)):ti,ab 328470
#55 (((anti NEXT infectiv*) or antiinfectiv* or antibacter* or (anti NEXT bacter*) or antimicrobial* or (anti NEXT microbial*) or antibiot* or (anti NEXT biot*) or (anti NEXT viral*) or antiviral*) NEAR/3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or (step* NEXT up) or (step* NEXT down) or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or rescue* or misuse* or overuse* or (over NEXT use*) or overprescri* or (over NEXT prescri*) or deprescri* or abus* or steward* or resist* or target* or spectrum* or narrow* or broad* or adjust* or modif* or prescrib* or prescription* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)):ti,ab 15125
#56 ((care* or treatment* or critical*) NEAR/2 (pathway* or path or paths)):ti,ab 1875
#57 ((mortality* or death*) NEAR/3 (predict* or risk* or prognos*)):ti,ab 14742
#58 ((severity* or severe* or nonsevere*) NEAR/3 (predict* or assess* or stratif* or risk*)):ti,ab 11302

Searches
#59 ((hospital* or healthcare* or (health NEXT care) or (secondary NEXT care*) or nosocomial*) NEAR/3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*) NEAR/3 (infect* or crossinfect* or (cross infect*))):ti,ab 1023
#60 ((prevent* or control*) NEAR/3 (infect* or crossinfect* or (cross NEXT infect*))):ti,ab 8937
#61 (Oseltamivir* or Tamiflu* or Ebilfumin*):ti,ab 605
#62 (risk* NEAR/1 (manag* or assess*)):ti,ab 6425
#63 {or #31-#62} 655232
#64 #30 and #63 1754
#65 ((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an498244
#66 #64 not #65 854
#67 "conference":pt 239278
#68 #66 not #67 700
#69 #66 not #67 in Trials 680
Post search filter: Date added to CENTRAL trials database: 01/03/2014 to 01/03/2024 411

Database name: Embase

Searches
1 pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ or hospital acquired pneumonia/ 320903
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 238026
3 1 or 2 404343
4 *microbiological examination/ 7326
5 (microbiolog* adj2 (test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or sample* or test* or swab* or culture* or screen* or smear* or specimen* or exam* or analys*)).ti,ab.25591
6 *blood culture/ 5481
7 ((blood* or serolog*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys*)).ti,ab. 532274
8 exp *sputum examination/ 3538
9 exp *throat culture/ 1483
10 ((sputum* or mucus* or phlegm* or saliva* or secretion* or oropharyn* or nasopharyn* or nasal* or nose* or pharynx* or pharyngeal* or throat* or trachea* or discharge*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or aspirat* or antigen* or exam* or analys*)).ti,ab. 119432

Searches
11 *urinalysis/ or *urine culture/ 14998
12 (urinalys* or UAT).ti,ab. 18474
13 (urin* adj3 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys* or legionella* or pneumococc*)).ti,ab. 144134
14 exp *bacterial antigen/ 20937
15 *gram staining/ 612
16 gram stain*.ti,ab. 15532
17 (bacteria* adj2 antigen*).ti,ab. 4133
18 *molecular diagnosis/ 8976
19 *molecular diagnostics/ 1848
20 *bacterium identification/ 13050
21 *bacterial load/ 1213
22 *virus load/ 7506
23 *nucleic acid amplification techniques/ 413
24 exp *polymerase chain reaction/ 66943
25 exp *loop mediated isothermal amplification/ 2927
26 (molecular* adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 145979
27 ((bacteria* or bacterium* or virus* or viral*) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 111451
28 ((bacteria* or bacterium* or virus* or viral*) adj1 (load* or burden*)).ti,ab. 84831
29 ((singleplex* or "single plex*" or multiplex* or "multi plex*") adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or molecular*)).ti,ab. 29926
30 ((Polymerase Chain Reaction* or PCR) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or singleplex* or "single plex*" or multiplex* or "multi plex*" or realtime* or "real time*")).ti,ab. 408124
31 (NAAT or NAATs or LAMP).ti,ab. 33559
32 (("Nucleic Acid*" or DNA or RNA or "loop mediated") adj1 (amplification* or amplify* or amplifies*)).ti,ab. 15673
33 (Filmarray* or "Film array*" or Unyvero* or "Fast Track Diagnostics respiratory panel*").ti,ab. 1351
34 or/4-33 1583168
35 3 and 34 42045
36 respiratory care/ or respiratory care practice/ or exp artificial ventilation/ 261420
37 hospitalization/ or hospital care/ or hospital patient/ or secondary health care/ 781356
38 emergency ward/ or high dependency unit/ or emergency health service/ or hospital emergency service/ or emergency treatment/ or emergency care/ or evidence based emergency medicine/ or emergency medicine/ 428680
39 intensive care/ or intensive care unit/ or medical intensive care unit/ 367360
40 clinical pathway/ or critical care outcome/ 10793
41 patient referral/ or patient triage/ 169284
42 clinical decision making/ or clinical practice/ or clinical handover/ 444146
43 patient acuity/ or hospital discharge/ or hospital admission/ or hospital readmission/ or retreatment/ 540990

Searches
44 treatment failure/ or treatment outcome/ or clinical outcome/ 1469544
45 exp mortality/ 1420425
46 drug administration/ or acute drug administration/ or treatment duration/ or "length of stay"/639408
47 unnecessary prescribing/ or overprescribing/ 540
48 antiinfective agent/ or exp antibiotic agent/ or antimicrobial therapy/ or anti-infective therapy/ or antibiotic therapy/ 2031135
49 antimicrobial stewardship/ or antibiotic resistance/ 209796
50 Infection Control/ or Cross Infection/ 119288
51 oseltamivir/ or antivirus agent/ 112074
52 risk assessment/ or health risk assessment/ or risk management/797373
53 (hospitaliz* or hospitalis* or rehospitalis* or rehospitaliz*).ti,ab. 587654
54 (hospital* adj3 ((stay* or episod*) adj3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))).ti,ab. 152500
55 ((hospital* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or "A&E" or "secondary care*" or "respiratory care*" or "accident and emergenc*") adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 604858
56 ((specialist* or specialized* or specialised* or emergenc* or secondary*) adj2 (care* or service* or facility* or facilities* or ward or wards or unit or units or department* or clinic or clinics) adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 40629
57 ((invasive* or artificial*) adj3 (respirat* or ventilat*)).ti,ab. 35209
58 ((discharg* or referral* or referred*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or interval* or schedul* or period* or threshold*)).ti,ab. 71343
59 (hospital* adj3 ((stay* or episod*) adj3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))).ti,ab. 152500
60 ("length* of stay*" or "episode* of care").ti,ab. 163917
61 ((therap* or intervention* or treatment*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 2415661
62 (("anti infectiv*" or antiinfectiv* or antibacter* or "anti bacter*" or antimicrobial* or "anti microbial*" or antibiot* or "anti biot*" or "anti viral*" or antiviral*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or rescue* or misuse* or overuse* or "over use*" or overprescri* or "over prescri*" or deprescri* or abus* or steward* or resist* or target* or spectrum* or narrow* or broad* or adjust* or modif* or prescrib* or prescription* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 331220

Searches
63 ((care* or treatment* or critical*) adj2 (pathway* or path or paths)).ti,ab. 41212
64 ((mortality* or death*) adj3 (predict* or risk* or prognos*)).ti,ab. 282071
65 ((severity* or severe* or nonsevere*) adj3 (predict* or assess* or stratif* or risk*)).ti,ab. 132486
66 ((hospital* or healthcare* or "health care*" or "secondary care*" or nosocomial*) adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 25786
67 ((prevent* or control*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 151720
68 (Oseltamivir* or Tamiflu* or Ebilfumin*).ti,ab. 6442
69 (risk* adj1 (manag* or assess*)).ti,ab. 161771
70 or/36-69 9169810
71 35 and 70 30153
72 limit 71 to english language 27838
73 (letter or editorial).pt. 2110164
74 72 not 73 27635
75 Case report/ 2975259
76 74 not 75 20775
77 nonhuman/ not human/ 5401002
78 76 not 77 18968
79 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5862600
80 78 not 79 11864
81 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ 1749946

Searches		
82	exp "organisation for economic co-operation and development"/ or exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ or european union/ or developed country/	3880914
83	81 not 82	1592902
84	80 not 83	10038
85	random:.tw.	2043130
86	placebo:.mp.	534860
87	double-blind:.tw.	250157
88	or/85-87	2325020
89	84 and 88	929
90	predict.ti.	102438
91	(validat* or rule*).ti,ab.	1369094
92	(predict* and (outcome* or risk* or model*)).ti,ab.	1716326
93	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.	5996647
94	decision*.ti,ab. and Statistical model/	8147
95	(decision* and (model* or clinical*)).ti,ab.	378658
96	(prognostic* and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.	488474
97	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.	1539641
98	Receiver operating characteristic/	224665
99	prognosis/ or prognostic assessment/	704280
100	or/90-99	8634245
101	84 and 100	4122
102	89 or 101	4718
103	limit 102 to dc=20140301-20240331	3178

Database name: MEDLINE ALL

Searches		
1	pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or healthcare-associated pneumonia/	124928
2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab.	162188
3	1 or 2	232142
4	Microbiological Techniques/	7277
5	(microbiolog* adj2 (test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or sample* or test* or swab* or culture* or screen* or smear* or specimen* or exam* or analys*)).ti,ab.	19000

Searches
6 Blood Culture/ 1851
7 ((blood* or serolog*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys*)).ti,ab. 345694
8 ((sputum* or mucus* or phlegm* or saliva* or secretion* or oropharyn* or nasopharyn* or nasal* or nose* or pharynx* or pharyngeal* or throat* or trachea* or discharge*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or aspirat* or antigen* or exam* or analys*)).ti,ab. 86973
9 urinalysis/ 9406
10 (urinalys* or UAT).ti,ab. 9955
11 (urin* adj3 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys* or legionella* or pneumococc*)).ti,ab. 98014
12 antigens, bacterial/ 45780
13 gram stain*.ti,ab. 11732
14 (bacteria* adj2 antigen*).ti,ab. 3553
15 Molecular Diagnostic Techniques/ 13888
16 exp Bacterial Typing Techniques/ 70472
17 Bacterial Load/ 6871
18 Viral Load/ 39310
19 Nucleic Acid Amplification Techniques/ 14219
20 exp Polymerase Chain Reaction/ 467590
21 (molecular* adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 109348
22 ((bacteria* or bacterium* or virus* or viral*) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 89605
23 ((bacteria* or bacterium* or virus* or viral*) adj1 (load* or burden*)).ti,ab. 57388
24 ((singleplex* or "single plex*" or multiplex* or "multi plex*") adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or molecular*)).ti,ab. 18653
25 ((Polymerase Chain Reaction* or PCR) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or singleplex* or "single plex*" or multiplex* or "multi plex*" or realtime* or "real time*")).ti,ab. 296992
26 (NAAT or NAATs or LAMP).ti,ab. 26951
27 (("Nucleic Acid*" or DNA or RNA or "loop mediated") adj1 (amplification* or amplify* or amplifies*)).ti,ab. 12560
28 (Filmarray* or "Film array*" or Unyvero* or "Fast Track Diagnostics respiratory panel*").ti,ab. 773
29 or/4-28 1522834
30 3 and 29 27339
31 Respiratory Care Units/ or Respiratory Therapy Department, Hospital/ or exp Respiratory therapy/ 136233
32 hospitalization/ or hospitals/ or secondary care/ 239988
33 Emergency Service, Hospital/ or Emergency Treatment/ or Emergency Medical Services/ or exp Emergency Medicine/ or Intensive Care Units/ 224855
34 Critical pathways/ or Critical Care/ 69506
35 "Referral and Consultation"/ or Triage/ or patient transfer/ or Patient Handoff/ or Gatekeeping/ 102444
36 Clinical Decision-Making/ or Practice Patterns, Physicians'/ 81563

Searches
37 Patient acuity/ or Patient Discharge/ or Patient Readmission/ or Retreatment/ 72821
38 Treatment Failure/ or Treatment Outcome/ 1210269
39 exp mortality/ 426092
40 Drug Administration Schedule/ or Duration of Therapy/ or Episode of Care/ or Length of Stay/ 209087
41 Inappropriate prescribing/ 4741
42 anti-infective agents/ or exp anti-bacterial agents/ or exp beta Lactam Antibiotics/ or Antimicrobial Stewardship/ 870057
43 Infection Control/ or Cross Infection/ 81351
44 Oseltamivir/ or Antiviral Agents/ 102782
45 risk assessment/ or risk management/ 327485
46 (hospitaliz* or hospitalis* or rehospitalis* or rehospitaliz*).ti,ab. 358433
47 ((patient* or inpatient*) adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or rebound* or revisit* or declin* or worsen* or remission* or deteriorat* or escalat* or deescalat* or acuity* or triage* or triaging* or morbidit* or handover* or handoff* or "hand over*" or "hand off*")).ti,ab. 408405
48 ((hospital* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or "A&E" or "secondary care*" or "respiratory care*" or "accident and emergenc*") adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 366124
49 ((specialist* or specialized* or specialised* or emergenc* or secondary*) adj2 (care* or service* or facility* or facilities* or ward or wards or unit or units or department* or clinic or clinics) adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 24647
50 ((invasive* or artificial*) adj3 (respirat* or ventilat*)).ti,ab. 21809
51 ((discharg* or referral* or referred*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or interval* or schedul* or period* or threshold*)).ti,ab. 41469
52 (hospital* adj3 ((stay* or episod*) adj3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))).ti,ab. 93455
53 ("length* of stay*" or "episode* of care").ti,ab. 88047
54 ((therap* or intervention* or treatment*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 1596072
55 (("anti infectiv*" or antiinfectiv* or antibacter* or "anti bacter*" or antimicrobial* or "anti microbial*" or antibiot* or "anti biot*" or "anti viral*" or antiviral*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or

Searches
admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or rescue* or misuse* or overuse* or "over use*" or overprescri* or "over prescri*" or deprescri* or abus* or steward* or resist* or target* or spectrum* or narrow* or broad* or adjust* or modif* or prescrib* or prescription* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 250010
56 ((care* or treatment* or critical*) adj2 (pathway* or path or paths)).ti,ab. 26536
57 ((mortality* or death*) adj3 (predict* or risk* or prognos*)).ti,ab. 181195
58 ((severity* or severe* or nonsevere*) adj3 (predict* or assess* or stratif* or risk*)).ti,ab. 84833
59 ((hospital* or healthcare* or "health care*" or "secondary care*" or nosocomial*) adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 18298
60 ((prevent* or control*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 118964
61 (Oseltamivir* or Tamiflu* or Ebilfumin*).ti,ab. 4510
62 (risk* adj1 (manag* or assess*)).ti,ab. 122456
63 or/31-62 5552434
64 30 and 63 14656
65 limit 64 to english language 12929
66 limit 65 to (letter or historical article or comment or editorial or news or case reports) 2449
67 65 not 66 10480
68 Animals/ not (Animals/ and Humans/) 5168485
69 67 not 68 9661
70 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ 1330757
71 "organisation for economic co-operation and development"/ or australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or

Searches
costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ or european union/ or developed countries/ 3553183
72 70 not 71 1240208
73 69 not 72 8163
74 exp Randomized Controlled Trial/ 611602
75 randomi?ed.mp. 1109176
76 placebo.mp. 254546
77 or/74-76 1176529
78 73 and 77 528
79 predict.ti. 67622
80 (validat* or rule*).ti,ab. 978250
81 (predict* and (outcome* or risk* or model*)).ti,ab. 1220557
82 ((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab. 4336205
83 decision*.ti,ab. and Logistic models/ 5946
84 (decision* and (model* or clinical*)).ti,ab. 261509
85 (prognostic* and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab. 315696
86 (stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab. 1142485
87 ROC curve/ 72222
88 Prognosis/ 607159
89 or/79-88 6425951
90 73 and 89 3302
91 78 or 90 3673
92 limit 91 to ed=20140301-20240331 1928
93 limit 91 to dt=20140301-20240331 2358
94 92 or 93 2433

Additional search techniques

Forward citation searching

Date of search	12/03/2024
How the seed papers were identified	Identified from the papers selected for this question from the search for systematic reviews; the scoping searches for this guideline; and the included papers in CG191.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present)

	• Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-03-09
How results were managed	A single search was done for the adults and children aspects of this review. Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.
How the results were selected	Included any papers potentially relevant to the microbiological tests listed in the protocol. Did not include any papers that were exclusively conducted in countries that are not members of the OECD. Did not include any papers about COVID-19, tuberculosis, sepsis, influenza or other conditions. Did not include any papers that were about methods or epidemiology. Did not include animal studies, letters or editorials. Did not include anything that was not written in English. Did not include anything published before 2014 if it was just about adults.
List of seed papers used	Benenson RS et al. (2007) Selective use of blood cultures in emergency department pneumonia patients. Journal of Emergency Medicine, 33(1),1-8 Buchan BW et al. (2021) Molecular diagnosis of pneumonia (including multiplex panels). Clinical Chemistry, 68(1), 59-68. Burk M et al. (2016) Viral infection in community-acquired pneumonia: a systematic review and meta-analysis. European Respiratory Review, 25(140), 178-88. Chan YR & Morris A (2007) Molecular diagnostic methods in pneumonia. Current Opinion in Infectious Diseases, 20(2), 157-64.

	Chen K et al. (2021) Accuracy of molecular amplification assays for diagnosis of staphylococcal pneumonia: a systematic review and meta-analysis. Journal of Clinical Microbiology, 59(8), e0300320. Dedier J et al. (2001) Processes of care, illness severity, and outcomes in the management of community-acquired pneumonia at academic hospitals. Archives of Internal Medicine, 161(17), 2099-2104 Del Rio-Pertuz G et al. (2019) Usefulness of sputum gram stain for etiologic diagnosis in community-acquired pneumonia: a systematic review and meta-analysis. BMC Infectious Diseases, 19(1), 403. Enne VI et al. (2022) Multicentre evaluation of two multiplex pcr platforms for the rapid microbiological investigation of nosocomial pneumonia in uk icus: the inhale wp1 study. Thorax, 77(12), 1220-1228. Falguera M et al. (2010) Prospective, randomised study to compare empirical treatment versus targeted treatment on the basis of the urine antigen results in hospitalised patients with community-acquired pneumonia. Thorax, 65(2), 101-106 Horita N et al. (2013) Sensitivity and specificity of the streptococcus pneumoniae urinary antigen test for unconcentrated urine from adult patients with pneumonia: a meta-analysis. Respirology, 18(8), 1177-83. Iroh Tam PY et al. (2015) Blood culture in evaluation of pediatric community-acquired pneumonia: a systematic review and meta-analysis. Hospital Pediatrics, 5(6), 324-36. Lee JS et al. (2011) Processes of care and outcomes for community-acquired pneumonia. American Journal of Medicine, 124(12), 1175-17 Lidman C et al. (2002) Limited value of routine microbiological diagnostics in patients hospitalized for community-acquired pneumonia. Scandinavian Journal of Infectious Diseases, 34(12), 873-879

	Meehan TP et al. (1997) Quality of care, process, and outcomes in elderly patients with pneumonia. Journal of the American Medical Association, 278(23), 2080-2084 Milas GP et al. (2022) Blood urea nitrogen to albumin ratio as a predictive factor for pneumonia: a meta-analysis. Respiratory Medical Research, 81, 100886. Moy AC et al. (2023) Performance evaluation of a pcr panel (filmarray r pneumonia plus) for detection of respiratory bacterial pathogens in respiratory specimens: a systematic review and meta-analysis. Anaesthesia Critical Care & Pain Medicine, 42(6), 101300. Ogawa H et al. (2020) Sputum gram stain for bacterial pathogen diagnosis in community-acquired pneumonia: a systematic review and bayesian meta-analysis of diagnostic accuracy and yield. Clinical Infectious Diseases, 71(3), 499-513. Ogawa H et al. (2019) Sputum gram stain for diagnosing causative bacterial pathogens and guiding antimicrobial therapies in community-acquired pneumonia: a systematic review and meta-analysis protocol. Fujita Medical Journal, 5(3), 79-84. Parente DM et al. (2018) The clinical utility of methicillin-resistant staphylococcus aureus (mrsa) nasal screening to rule out mrsa pneumonia: a diagnostic meta-analysis with antimicrobial stewardship implications. Clinical Infectious Diseases, 67(1), 1-7. Piso RJ et al. (2012) The routine use of the urinary pneumococcal antigen test in hospitalised patients with community acquired pneumonia has limited impact for adjustment of antibiotic treatment. Swiss Medical Weekly, 142 Poole S & Clark TW (2020) Rapid syndromic molecular testing in pneumonia: the current landscape and future potential. Journal of Infection, 80(1), 1-7.

	Poole S et al. (2022) Molecular point-of-care testing for lower respiratory tract pathogens improves safe antibiotic de-escalation in patients with pneumonia in the icu: results of a randomised controlled trial.. Journal of Infection, 85(6), 625-633. Serigstad S et al. (2022) Impact of rapid molecular testing on diagnosis, treatment and management of community-acquired pneumonia in norway: a pragmatic randomised controlled trial (capnor). Trials, 23(1), 622. Sinclair A et al. (2013) Systematic review and meta-analysis of a urine-based pneumococcal antigen test for diagnosis of community-acquired pneumonia caused by streptococcus pneumoniae. Journal of Clinical Microbiology, 51(7), 2303-10. Uematsu H et al. (2014) Impact of guideline-concordant microbiological testing on outcomes of pneumonia. International Journal for Quality in Health Care, 26(1), 100-107 van der Eerden MM et al. (2005) Comparison between pathogen directed antibiotic treatment and empirical broad spectrum antibiotic treatment in patients with community acquired pneumonia: a prospective randomised study. Thorax, 60(8), 672-678 Voiriot G et al.(2021) Combined use of a broad-panel respiratory multiplex PCR and procalcitonin to reduce duration of antibiotics exposure in patients with severe community-acquired pneumonia (MULTI-CAP): a multicentre, parallel-group, open-label, individual randomised trial conducted in French intensive care units. BMJ Open, 11(8), e048187. Wang Y et al. (2018) Serum tumor necrosis factor-alpha and interferon-γ levels in pediatric mycoplasma pneumoniae pneumonia: a systematic review and meta-analysis. Canadian Respiratory Journal, 2018, 8354892. Yasuo S et al. (2022) 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, 12(8), e057216.
No. of results	93

Reference list checking

Date of search	12/03/2024
How the seed papers were identified	Identified from the papers selected for this question from the search for systematic reviews; the scoping searches for this guideline; and the included papers in CG191.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-03-09
How results were managed	A single search was done for the adults and children aspects of this review. Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.
How the results were selected	Included any papers potentially relevant to the microbiological tests listed in the protocol. Did not include any papers that were exclusively conducted in countries that are not members of the OECD. Did not include any papers about COVID-19, tuberculosis, sepsis, influenza or other conditions. Did not include any papers that were about methods or epidemiology. Did not include animal studies, letters or editorials. Did not include anything that was not written in English. Did not include anything published before 2014 if it was just about adults.

List of seed papers used	Buchan BW et al. (2021) Molecular diagnosis of pneumonia (including multiplex panels). Clinical Chemistry, 68(1), 59-68. Burk M et al. (2016) Viral infection in community-acquired pneumonia: a systematic review and meta-analysis. European Respiratory Review, 25(140), 178-88. Chen K et al. (2021) Accuracy of molecular amplification assays for diagnosis of staphylococcal pneumonia: a systematic review and meta-analysis. Journal of Clinical Microbiology, 59(8), e0300320. Del Rio-Pertuz G et al. (2019) Usefulness of sputum gram stain for etiologic diagnosis in community-acquired pneumonia: a systematic review and meta-analysis. BMC Infectious Diseases, 19(1), 403. Enne VI et al. (2022) Multicentre evaluation of two multiplex pcr platforms for the rapid microbiological investigation of nosocomial pneumonia in uk icus: the inhale wp1 study. Thorax, 77(12), 1220-1228. Iroh Tam PY et al. (2015) Blood culture in evaluation of pediatric community-acquired pneumonia: a systematic review and meta-analysis. Hospital Pediatrics, 5(6), 324-36. Milas GP et al. (2022) Blood urea nitrogen to albumin ratio as a predictive factor for pneumonia: a meta-analysis. Respiratory Medical Research, 81, 100886. Moy AC et al. (2023) Performance evaluation of a pcr panel (filmarray r pneumonia plus) for detection of respiratory bacterial pathogens in respiratory specimens: a systematic review and meta-analysis. Anaesthesia Critical Care & Pain Medicine, 42(6), 101300. Ogawa H et al. (2020) Sputum gram stain for bacterial pathogen diagnosis in community-acquired pneumonia: a systematic review and bayesian meta-analysis of diagnostic accuracy and yield. Clinical Infectious Diseases, 71(3), 499-513.

	Ogawa H et al. (2019) Sputum gram stain for diagnosing causative bacterial pathogens and guiding antimicrobial therapies in community-acquired pneumonia: a systematic review and meta-analysis protocol. Fujita Medical Journal, 5(3), 79-84. Parente DM et al. (2018) The clinical utility of methicillin-resistant staphylococcus aureus (mrsa) nasal screening to rule out mrsa pneumonia: a diagnostic meta-analysis with antimicrobial stewardship implications. Clinical Infectious Diseases, 67(1), 1-7. Poole S & Clark TW (2020) Rapid syndromic molecular testing in pneumonia: the current landscape and future potential. Journal of Infection, 80(1), 1-7. Poole S et al. (2022) Molecular point-of-care testing for lower respiratory tract pathogens improves safe antibiotic de-escalation in patients with pneumonia in the icu: results of a randomised controlled trial.. Journal of Infection, 85(6), 625-633. Serigstad S et al. (2022) Impact of rapid molecular testing on diagnosis, treatment and management of community-acquired pneumonia in norway: a pragmatic randomised controlled trial (capnor). Trials, 23(1), 622. Voiriot G et al.(2021) Combined use of a broad-panel respiratory multiplex PCR and procalcitonin to reduce duration of antibiotics exposure in patients with severe community-acquired pneumonia (MULTI-CAP): a multicentre, parallel-group, open-label, individual randomised trial conducted in French intensive care units. BMJ Open, 11(8), e048187. Wang Y et al. (2018) Serum tumor necrosis factor-alpha and interferon-γ levels in pediatric mycoplasma pneumoniae pneumonia: a systematic review and meta-analysis. Canadian Respiratory Journal, 2018, 8354892. Yasuo S et al. (2022) 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, 12(8), e057216.
No. of results	85

Contact with experts post search

Date of search	19/12/2024
How the seed papers were identified	In line with section 6.1 of the NICE manual (Ensuring relevant records are not missed) a new paper notified by an expert was considered for screening for Part 2A.
How results were managed	The study was added manually to EPPI-Reviewer using the PubMed record.
No. of results	1
Seed paper considered	Virk A et al. (2024) Rapid multiplex PCR panel for pneumonia in hospitalised patients with suspected pneumonia in the USA: a single-centre, open-label, pragmatic, randomised controlled trial. The Lancet Microbe, 5(12), 100928.

Part 2B: Effectiveness and prognostic evidence searches (children)

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	13/03/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 2 of 12, February 2024	214
Embase	13/03/2024	Ovid	Embase 1974 to 2024 March 12	1285
MEDLINE ALL	13/03/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to March 12, 2024	1000

Search strategy history

Database name: Cochrane Central Register of Controlled Trials (CENTRAL)

Searches
#1 [mh ^pneumonia] or [mh ^bronchopneumonia] or [mh ^pleuropneumonia] or [mh ^"pneumonia, bacterial"] or [mh ^"chlamydial pneumonia"] or [mh ^"pneumonia, mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, staphylococcal"]

Searches
or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 4399
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15670
#3 #1 or #2 16911
#4 [mh ^"Microbiological Techniques"] 58
#5 (microbiolog* NEAR/2 (test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or sample* or test* or swab* or culture* or screen* or smear* or specimen* or exam* or analys*)):ti,ab 1775
#6 [mh ^"Blood Culture"] 44
#7 ((blood* or serolog*) NEAR/2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys*)):ti,ab 58281
#8 ((sputum* or mucus* or phlegm* or saliva* or secretion* or oropharyn* or nasopharyn* or nasal* or nose* or pharynx* or pharyngeal* or throat* or trachea* or discharge*) NEAR/2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or aspirat* or antigen* or exam* or analys*)):ti,ab 11287
#9 [mh ^urinalysis] 336
#10 (urinalys* or UAT):ti,ab 3478
#11 (urin* NEAR/3 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys* or legionella* or pneumococc*)):ti,ab 17220
#12 [mh ^"antigens, bacterial"] 516
#13 gram stain*:ti,ab 566
#14 (bacteria* NEAR/2 antigen*):ti,ab 65
#15 [mh ^"Molecular Diagnostic Techniques"] 125
#16 [mh "Bacterial Typing Techniques"] 338
#17 [mh ^"Bacterial Load"] 488
#18 [mh ^"Viral Load"] 3363
#19 [mh ^"Nucleic Acid Amplification Techniques"] 74
#20 [mh "Polymerase Chain Reaction"] 2834
#21 (molecular* NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)):ti,ab 1491
#22 ((bacteria* or bacterium* or virus* or viral*) NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)):ti,ab 2813
#23 ((bacteria* or bacterium* or virus* or viral*) NEAR/1 (load* or burden*)):ti,ab 7511
#24 ((singleplex* or (single NEXT plex*) or multiplex* or (multi NEXT plex*)) NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or molecular*)):ti,ab 835
#25 (((Polymerase Chain NEXT Reaction*) or PCR) NEAR/3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or singleplex* or (single NEXT plex*) or multiplex* or (multi NEXT plex*) or realtime* or (real NEXT time*))):ti,ab 6366
#26 (NAAT or NAATs or LAMP):ti,ab 2316
#27 (((Nucleic NEXT Acid*) or DNA or RNA or "loop mediated") NEAR/1 (amplification* or amplify* or amplifies*)):ti,ab 298
#28 (Filmarray* or (Film NEXT array*) or Unyvero* or "Fast Track Diagnostics respiratory panel"):ti,ab 84

Searches
#29 {or #4-#28} 105370
#30 #3 and #29 2367
#31 [mh ^"Respiratory Care Units"] or [mh ^"Respiratory Therapy Department, Hospital"] or [mh "Respiratory therapy"] 12054
#32 [mh ^hospitalization] or [mh ^hospitals] or [mh ^"secondary care"]9260
#33 [mh ^"Emergency Service, Hospital"] or [mh ^"Emergency Treatment"] or [mh ^"Emergency Medical Services"] or [mh "Emergency Medicine"] or [mh ^"Intensive Care Units"] 9512
#34 [mh ^"critical pathways"] or [mh ^"Critical Care"] 2960
#35 [mh ^"Referral and Consultation"] or [mh ^Triage] or [mh ^"patient transfer"] or [mh ^"Patient Handoff"] or [mh ^Gatekeeping] 3506
#36 [mh ^"Clinical Decision-Making"] or [mh ^"Practice Patterns, Physicians'"] 2656
#37 [mh ^"Patient acuity"] or [mh ^"Patient Discharge"] or [mh ^"Patient Readmission"] or [mh ^Retreatment] 5259
#38 [mh ^"Treatment Failure"] or [mh ^"Treatment Outcome"] 193930
#39 [mh mortality] 18860
#40 [mh ^"Drug Administration Schedule"] or [mh ^"Duration of Therapy"] or [mh ^"Episode of Care"] or [mh ^"Length of Stay"] 37835
#41 [mh ^"Inappropriate prescribing"] 279
#42 [mh ^"anti-infective agents"] or [mh "anti-bacterial agents"] or [mh "beta Lactam Antibiotics"] or [mh "Antimicrobial Stewardship"] 19450
#43 [mh ^"Infection Control"] or [mh ^"Cross Infection"] 2175
#44 [mh ^Oseltamivir] or [mh ^"Antiviral Agents"] 5806
#45 [mh ^"risk assessment"] or [mh ^"risk management"] 13651
#46 (hospitaliz* or hospitalis* or rehospitalis* or rehospitaliz*):ti,ab 61219
#47 ((patient* or inpatient*) NEAR/3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or rebound* or revisit* or declin* or worsen* or remission* or deteriorat* or escalat* or deescalat* or acuity* or triage* or triaging* or morbidit* or handover* or handoff* or (hand NEXT over*) or (hand NEXT off*))):ti,ab 54825
#48 ((hospital* or ICU or (intensive NEXT care*) or (intensive NEXT treatment*) or ITU or (high NEXT dependency*) or HDU or (critical NEXT care*) or "A&E" or (secondary NEXT care*) or (respiratory NEXT care*) or (accident near/1 emergenc*)) NEAR/3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)):ti,ab 61099
#49 ((specialist* or specialized* or specialised* or emergenc* or secondary*) NEAR/2 (care* or service* or facility* or facilities* or ward or wards or unit or units or department* or clinic or clinics) NEAR/3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)):ti,ab2908
#50 ((invasive* or artificial*) NEAR/3 (respirat* or ventilat*)):ti,ab 4940
#51 ((discharg* or referral* or referred*) NEAR/3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or interval* or schedul* or period* or threshold*)):ti,ab 9978
#52 (hospital* NEAR/3 ((stay* or episod*) NEAR/3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))):ti,ab 22448

Searches
#53 ("length of stay" or "episode of care"):ti,ab 13960
#54 ((therap* or intervention* or treatment*) NEAR/3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or (step* NEXT up) or (step* NEXT down) or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)):ti,ab 328470
#55 (((anti NEXT infectiv*) or antiinfectiv* or antibacter* or (anti NEXT bacter*) or antimicrobial* or (anti NEXT microbial*) or antibiot* or (anti NEXT biot*) or (anti NEXT viral*) or antiviral*) NEAR/3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or (step* NEXT up) or (step* NEXT down) or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or rescue* or misuse* or overuse* or (over NEXT use*) or overprescri* or (over NEXT prescri*) or deprescri* or abus* or steward* or resist* or target* or spectrum* or narrow* or broad* or adjust* or modif* or prescrib* or prescription* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)):ti,ab 15125
#56 ((care* or treatment* or critical*) NEAR/2 (pathway* or path or paths)):ti,ab 1875
#57 ((mortality* or death*) NEAR/3 (predict* or risk* or prognos*)):ti,ab 14742
#58 ((severity* or severe* or nonsevere*) NEAR/3 (predict* or assess* or stratif* or risk*)):ti,ab 11302
#59 ((hospital* or healthcare* or (health NEXT care) or (secondary NEXT care*) or nosocomial*) NEAR/3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*) NEAR/3 (infect* or crossinfect* or (cross infect*))):ti,ab 1023
#60 ((prevent* or control*) NEAR/3 (infect* or crossinfect* or (cross NEXT infect*))):ti,ab 8937
#61 (Oseltamivir* or Tamiflu* or Ebilfumin*):ti,ab 605
#62 (risk* NEAR/1 (manag* or assess*)):ti,ab 6425
#63 {or #31-#62} 655232
#64 #30 and #63 1754
#65 [mh "pediatrics"] or [mh ^Infant] or [mh ^"Infant Health"] or [mh ^"Infant Welfare"] or [mh ^"Infant Care"] or [mh Child] or [mh "Child Behavior"] or [mh ^"Child Health"] or [mh ^"Child Welfare"] or [mh ^"Child Care"] or [mh ^Minors] or [mh ^" Child, Hospitalized"] 94452
#66 (pediatric* or paediatric* or infan* or baby* or babies or toddler* or (pre NEXT school*) or preschool* or kindergar* or child* or minor or minors or boy* or girl* or kid or kids):ti,ab 236190
#67 [mh ^Adolescent] or [mh ^"Adolescent Behavior"] or [mh ^"Adolescent Health"] or [mh ^Puberty] or [mh ^"Adolescent, Hospitalized"] 136635
#68 ((under NEXT 18*) or (under NEXT eighteen*)):ti,ab 16890
#69 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or (school NEXT age*) or schoolage* or underage* or (under NEXT age*)):ti,ab 51523
#70 (young* NEAR/1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)):ti,ab 29578

Searches		
#71	{or #65-#70}	393205
#72	#64 and #71	508
#73	((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an	498244
#74	#72 not #73	259
#75	"conference":pt	239278
#76	#74 not #75	224
#77	#74 not #75 in Trials	214

Database name: Embase

Searches		
1	pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ or hospital acquired pneumonia/	320903
2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab.	238026
3	1 or 2	404343
4	*microbiological examination/	7326
5	(microbiolog* adj2 (test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or sample* or test* or swab* or culture* or screen* or smear* or specimen* or exam* or analys*)).ti,ab.	25591
6	*blood culture/	5481
7	((blood* or serolog*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys*)).ti,ab.	532274
8	exp *sputum examination/	3538
9	exp *throat culture/	1483
10	((sputum* or mucus* or phlegm* or saliva* or secretion* or oropharyn* or nasopharyn* or nasal* or nose* or pharynx* or pharyngeal* or throat* or trachea* or discharge*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or aspirat* or antigen* or exam* or analys*)).ti,ab.	119432
11	*urinalysis/ or *urine culture/	14998
12	(urinalys* or UAT).ti,ab.	18474
13	(urin* adj3 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys* or legionella* or pneumococc*)).ti,ab.	144134
14	exp *bacterial antigen/	20937
15	*gram staining/	612
16	gram stain*.ti,ab.	15532
17	(bacteria* adj2 antigen*).ti,ab.	4133
18	*molecular diagnosis/	8976

Searches
19 *molecular diagnostics/ 1848
20 *bacterium identification/ 13050
21 *bacterial load/ 1213
22 *virus load/ 7506
23 *nucleic acid amplification techniques/ 413
24 exp *polymerase chain reaction/ 66943
25 exp *loop mediated isothermal amplification/ 2927
26 (molecular* adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 145979
27 ((bacteria* or bacterium* or virus* or viral*) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 111451
28 ((bacteria* or bacterium* or virus* or viral*) adj1 (load* or burden*)).ti,ab. 84831
29 ((singleplex* or "single plex*" or multiplex* or "multi plex*") adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or molecular*)).ti,ab. 29926
30 ((Polymerase Chain Reaction* or PCR) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or singleplex* or "single plex*" or multiplex* or "multi plex*" or realtime* or "real time*")).ti,ab. 408124
31 (NAAT or NAATs or LAMP).ti,ab. 33559
32 (("Nucleic Acid*" or DNA or RNA or "loop mediated") adj1 (amplification* or amplify* or amplifies*)).ti,ab. 15673
33 (Filmarray* or "Film array*" or Unyvero* or "Fast Track Diagnostics respiratory panel*").ti,ab. 1351
34 or/4-33 1583168
35 3 and 34 42045
36 respiratory care/ or respiratory care practice/ or exp artificial ventilation/ 261420
37 hospitalization/ or hospital care/ or hospital patient/ or secondary health care/ 781356
38 emergency ward/ or high dependency unit/ or emergency health service/ or hospital emergency service/ or emergency treatment/ or emergency care/ or evidence based emergency medicine/ or emergency medicine/ 428680
39 intensive care/ or intensive care unit/ or medical intensive care unit/ 367360
40 clinical pathway/ or critical care outcome/ 10793
41 patient referral/ or patient triage/ 169284
42 clinical decision making/ or clinical practice/ or clinical handover/ 444146
43 patient acuity/ or hospital discharge/ or hospital admission/ or hospital readmission/ or retreatment/ 540990
44 treatment failure/ or treatment outcome/ or clinical outcome/ 1469544
45 exp mortality/ 1420425
46 drug administration/ or acute drug administration/ or treatment duration/ or "length of stay"/639408
47 unnecessary prescribing/ or overprescribing/ 540
48 antiinfective agent/ or exp antibiotic agent/ or antimicrobial therapy/ or anti-infective therapy/ or antibiotic therapy/ 2031135
49 antimicrobial stewardship/ or antibiotic resistance/ 209796
50 Infection Control/ or Cross Infection/ 119288

Searches
51 oseltamivir/ or antivirus agent/ 112074
52 risk assessment/ or health risk assessment/ or risk management/ 797373
53 (hospitaliz* or hospitalis* or rehospitalis* or rehospitaliz*).ti,ab. 587654
54 (hospital* adj3 ((stay* or episod*) adj3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))).ti,ab. 152500
55 ((hospital* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or "A&E" or "secondary care*" or "respiratory care*" or "accident and emergenc*") adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 604858
56 ((specialist* or specialized* or specialised* or emergenc* or secondary*) adj2 (care* or service* or facility* or facilities* or ward or wards or unit or units or department* or clinic or clinics) adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 40629
57 ((invasive* or artificial*) adj3 (respirat* or ventilat*)).ti,ab. 35209
58 ((discharg* or referral* or referred*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or interval* or schedul* or period* or threshold*)).ti,ab. 71343
59 (hospital* adj3 ((stay* or episod*) adj3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))).ti,ab. 152500
60 ("length* of stay*" or "episode* of care").ti,ab. 163917
61 ((therap* or intervention* or treatment*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 2415661
62 (("anti infectiv*" or antiinfectiv* or antibacter* or "anti bacter*" or antimicrobial* or "anti microbial*" or antibiot* or "anti biot*" or "anti viral*" or antiviral*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or rescue* or misuse* or overuse* or "over use*" or overprescri* or "over prescri*" or deprescri* or abus* or steward* or resist* or target* or spectrum* or narrow* or broad* or adjust* or modif* or prescrib* or prescription* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 331220
63 ((care* or treatment* or critical*) adj2 (pathway* or path or paths)).ti,ab. 41212
64 ((mortality* or death*) adj3 (predict* or risk* or prognos*)).ti,ab. 282071
65 ((severity* or severe* or nonsevere*) adj3 (predict* or assess* or stratif* or risk*)).ti,ab. 132486
66 ((hospital* or healthcare* or "health care*" or "secondary care*" or nosocomial*) adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 25786
67 ((prevent* or control*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 151720

Searches
68 (Oseltamivir* or Tamiflu* or Ebilfumin*).ti,ab. 6442
69 (risk* adj1 (manag* or assess*)).ti,ab. 161771
70 or/36-69 9169810
71 35 and 70 30153
72 exp pediatrics/ or Juvenile/ or exp child/ or child health/ or infant welfare/ or Child Behavior/ or Child Welfare/ or exp child care/ or "minor (person)"/ or hospitalized child/ or hospitalized infant/ or child hospitalization/ 3307064
73 pediatric hospital/ or pediatric ward/ or pediatric intensive care unit/ 52219
74 (pediatric* or paediatric* or infan* or baby* or babies or toddler* or "pre school*" or preschool* or kindergar* or child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 3369239
75 exp adolescent/ or adolescent behavior/ or adolescent health/ or exp Puberty/ or hospitalized adolescent/ 1858735
76 elementary student/ or high school student/ or middle school student/ 13542
77 ("under 18*" or "under eighteen*").ti,ab. 7849
78 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or "school age*" or schoolage* or underage* or "under age*").ti,ab. 787236
79 (young* adj1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)).ti,ab. 478436
80 or/72-79 5637019
81 71 and 80 8548
82 limit 81 to english language 7798
83 (letter or editorial).pt. 2110164
84 82 not 83 7769
85 Case report/ 2975259
86 84 not 85 6114
87 nonhuman/ not human/ 5401002
88 86 not 87 5973
89 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5862600
90 88 not 89 4335
91 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or

Searches	
philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/	1749946
92 exp "organisation for economic co-operation and development"/ or exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ or european union/ or developed country/	3880914
93 91 not 92	1592902
94 90 not 93	3215
95 random:.tw.	2043130
96 placebo:.mp.	534860
97 double-blind:.tw.	250157
98 or/95-97	2325020
99 94 and 98	230
100 predict.ti.	102438
101 (validat* or rule*).ti,ab.	1369094
102 (predict* and (outcome* or risk* or model*)).ti,ab.	1716326
103 ((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.	5996647
104 decision*.ti,ab. and Statistical model/	8147
105 (decision* and (model* or clinical*)).ti,ab.	378658
106 (prognostic* and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.	488474
107 (stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.	1539641
108 Receiver operating characteristic/	224665
109 prognosis/ or prognostic assessment/	704280
110 or/100-109	8634245
111 94 and 110	1145
112 99 or 111	1285

Database name: MEDLINE ALL

Searches	
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or healthcare-associated pneumonia/	124928

Searches
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 162188
3 1 or 2 232142
4 Microbiological Techniques/ 7277
5 (microbiolog* adj2 (test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or sample* or test* or swab* or culture* or screen* or smear* or specimen* or exam* or analys*)).ti,ab. 19000
6 Blood Culture/ 1851
7 ((blood* or serolog*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys*)).ti,ab. 345694
8 ((sputum* or mucus* or phlegm* or saliva* or secretion* or oropharyn* or nasopharyn* or nasal* or nose* or pharynx* or pharyngeal* or throat* or trachea* or discharge*) adj2 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or aspirat* or antigen* or exam* or analys*)).ti,ab. 86973
9 urinalysis/ 9406
10 (urinalys* or UAT).ti,ab. 9955
11 (urin* adj3 (sample* or test* or swab* or culture* or screen* or smear* or specimen* or antigen* or exam* or analys* or legionella* or pneumococc*)).ti,ab. 98014
12 antigens, bacterial/ 45780
13 gram stain*.ti,ab. 11732
14 (bacteria* adj2 antigen*).ti,ab. 3553
15 Molecular Diagnostic Techniques/ 13888
16 exp Bacterial Typing Techniques/ 70472
17 Bacterial Load/ 6871
18 Viral Load/ 39310
19 Nucleic Acid Amplification Techniques/ 14219
20 exp Polymerase Chain Reaction/ 467590
21 (molecular* adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 109348
22 ((bacteria* or bacterium* or virus* or viral*) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic*)).ti,ab. 89605
23 ((bacteria* or bacterium* or virus* or viral*) adj1 (load* or burden*)).ti,ab. 57388
24 ((singleplex* or "single plex*" or multiplex* or "multi plex*") adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or molecular*)).ti,ab. 18653
25 ((Polymerase Chain Reaction* or PCR) adj3 (typing* or identif* or test* or technique* or panel* or platform* or assay* or immunoassay* or syndromic* or singleplex* or "single plex*" or multiplex* or "multi plex*" or realtime* or "real time*")).ti,ab. 296992
26 (NAAT or NAATs or LAMP).ti,ab. 26951
27 (("Nucleic Acid*" or DNA or RNA or "loop mediated") adj1 (amplification* or amplify* or amplifies*)).ti,ab. 12560
28 (Filmarray* or "Film array*" or Unyvero* or "Fast Track Diagnostics respiratory panel*").ti,ab. 773
29 or/4-28 1522834
30 3 and 29 27339
31 Respiratory Care Units/ or Respiratory Therapy Department, Hospital/ or exp Respiratory therapy/ 136233

Searches
32 hospitalization/ or hospitals/ or secondary care/ 239988
33 Emergency Service, Hospital/ or Emergency Treatment/ or Emergency Medical Services/ or exp Emergency Medicine/ or Intensive Care Units/ 224855
34 Critical pathways/ or Critical Care/ 69506
35 "Referral and Consultation"/ or Triage/ or patient transfer/ or Patient Handoff/ or Gatekeeping/ 102444
36 Clinical Decision-Making/ or Practice Patterns, Physicians'/ 81563
37 Patient acuity/ or Patient Discharge/ or Patient Readmission/ or Retreatment/ 72821
38 Treatment Failure/ or Treatment Outcome/ 1210269
39 exp mortality/ 426092
40 Drug Administration Schedule/ or Duration of Therapy/ or Episode of Care/ or Length of Stay/ 209087
41 Inappropriate prescribing/ 4741
42 anti-infective agents/ or exp anti-bacterial agents/ or exp beta Lactam Antibiotics/ or Antimicrobial Stewardship/ 870057
43 Infection Control/ or Cross Infection/ 81351
44 Oseltamivir/ or Antiviral Agents/ 102782
45 risk assessment/ or risk management/ 327485
46 (hospitaliz* or hospitalis* or rehospitalis* or rehospitaliz*).ti,ab. 358433
47 ((patient* or inpatient*) adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or rebound* or revisit* or declin* or worsen* or remission* or deteriorat* or escalat* or deescalat* or acuity* or triage* or triaging* or morbidit* or handover* or handoff* or "hand over*" or "hand off*")).ti,ab. 408405
48 ((hospital* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or "A&E" or "secondary care*" or "respiratory care*" or "accident and emergenc*") adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 366124
49 ((specialist* or specialized* or specialised* or emergenc* or secondary*) adj2 (care* or service* or facility* or facilities* or ward or wards or unit or units or department* or clinic or clinics) adj3 (admission* or admit* or transfer* or transition* or referral* or referred* or consultation* or consulting* or gatekeep* or postdischarg* or discharg* or retreat* or readmission* or readmit* or revisit* or escalat* or deescalat* or triage* or triaging* or duration* or length* or episod* or avoid*)).ti,ab. 24647
50 ((invasive* or artificial*) adj3 (respirat* or ventilat*)).ti,ab. 21809
51 ((discharg* or referral* or referred*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or interval* or schedul* or period* or threshold*)).ti,ab. 41469
52 (hospital* adj3 ((stay* or episod*) adj3 (time* or timing* or duration* or length* or short* or medium* or long* or prolong* or extend* or period*))).ti,ab. 93455
53 ("length* of stay*" or "episode* of care").ti,ab. 88047
54 ((therap* or intervention* or treatment*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or admin* or schedul* or

Searches
threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 1596072
55 (("anti infectiv*" or antiinfectiv* or antibacter* or "anti bacter*" or antimicrobial* or "anti microbial*" or antibiot* or "anti biot*" or "anti viral*" or antiviral*) adj3 (decision* or appropriat* or inappropriat* or defer* or delay* or optim* or immediate* or rapid* or accelerat* or fast* or slow* or time* or timing* or duration* or length* or short* or medium* or long* or episod* or extend* or prolong* or interval* or gradual* or persist* or escalat* or deescalat* or "step* up" or "step* down" or stepup or stepdown or fail* or outcome* or admin* or schedul* or threshold* or initiat* or start* or strateg* or unnecessar* or standby or "stand by" or avoid* or rescue* or misuse* or overuse* or "over use*" or overprescri* or "over prescri*" or deprescri* or abus* or steward* or resist* or target* or spectrum* or narrow* or broad* or adjust* or modif* or prescrib* or prescription* or continu* or discontinu* or rational* or pathogen* or guide* or guiding*)).ti,ab. 250010
56 ((care* or treatment* or critical*) adj2 (pathway* or path or paths)).ti,ab. 26536
57 ((mortality* or death*) adj3 (predict* or risk* or prognos*)).ti,ab. 181195
58 ((severity* or severe* or nonsevere*) adj3 (predict* or assess* or stratif* or risk*)).ti,ab. 84833
59 ((hospital* or healthcare* or "health care*" or "secondary care*" or nosocomial*) adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 18298
60 ((prevent* or control*) adj3 (infect* or crossinfect* or "cross infect*")).ti,ab. 118964
61 (Oseltamivir* or Tamiflu* or Ebilfumin*).ti,ab. 4510
62 (risk* adj1 (manag* or assess*)).ti,ab. 122456
63 or/31-62 5552434
64 30 and 63 14656
65 exp pediatrics/ or Infant/ or Infant Health/ or Infant Welfare/ or Infant Care/ or exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ or Child Care/ or Minors/ or Child, Hospitalized/ 2506282
66 (pediatric* or paediatric* or infan* or baby* or babies or toddler* or "pre school*" or preschool* or kindergar* or child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2654888
67 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ or Puberty/ or Adolescent, Hospitalized/ 2242885
68 ("under 18*" or "under eighteen*").ti,ab. 4453
69 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or "school age*" or schoolage* or underage* or "under age*").ti,ab. 614565
70 (young* adj1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)).ti,ab. 349509
71 or/65-70 5029855
72 64 and 71 4674
73 limit 72 to english language 4069
74 limit 73 to (letter or historical article or comment or editorial or news or case reports) 555
75 73 not 74 3514
76 Animals/ not (Animals/ and Humans/) 5168485
77 75 not 76 3480
78 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or

Searches
andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ 1330757
79 "organisation for economic co-operation and development"/ or australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ or european union/ or developed countries/ 3553183
80 78 not 79 1240208
81 77 not 80 2538
82 exp Randomized Controlled Trial/ 611602
83 randomi?ed.mp. 1109176
84 placebo.mp. 254546
85 or/82-84 1176529
86 81 and 85 139
87 predict.ti. 67622
88 (validat* or rule*).ti,ab. 978250
89 (predict* and (outcome* or risk* or model*)).ti,ab. 1220557
90 ((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab. 4336205
91 decision*.ti,ab. and Logistic models/ 5946
92 (decision* and (model* or clinical*)).ti,ab. 261509
93 (prognostic* and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab. 315696
94 (stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab. 1142485

Searches		
95	ROC curve/	72222
96	Prognosis/	607159
97	or/87-96	6425951
98	81 and 97	894
99	86 or 98	1000

Part 3: Cost effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Econlit	20/11/2023	Ovid	Econlit 1886 to November 11, 2023	90
Embase	20/11/2023	Ovid	Embase 1974 to 2023 November 17	2288
International HTA Database	20/11/2023	INAHTA	Version available on 20/11/23 with 21319 records	30
MEDLINE ALL	20/11/2023	Ovid	Ovid MEDLINE(R) ALL 1946 to November 17, 2023	1534
NHS Economic Evaluation Database (NHS EED)	20/11/2023	CRD	Archived – last updated 31 March 2015	11

Re-run results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Econlit	14/10/2024	Ovid	Econlit 1886 to October 03, 2024	6
Embase	14/10/2024	Ovid	Embase 1974 to 2024 October 11	306
International HTA Database	14/10/2024	INAHTA	Version available on 14/10/24 with 23533 records	6
MEDLINE ALL	14/10/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to	157

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
			October 11, 2024	

Search strategy history

Database name: Econlit

Searches		
1	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).af.	150
2	limit 1 to yr="2014 -Current"	90
Note: in the re-run Line 2 was changed to limit 1 to yr="2023 -Current".		

Database name: Embase

Searches		
1	pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or exp organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or hospital acquired pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or rickettsial pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/	314875
2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab.	232562
3	1 or 2	395881
4	cost utility analysis/	12471
5	quality adjusted life year/	35716
6	cost*.ti.	195365
7	(cost* adj2 utilit*).tw.	12784
8	(cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw.	385741
9	(economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw.	66452
10	(qualit* adj2 adjust* adj2 life*).tw.	27335
11	QALY*.tw.	26801
12	(incremental* adj2 cost*).tw.	28720
13	ICER.tw.	13032
14	utilities.tw.	15135
15	markov*.tw.	40152
16	(dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw.	72706
17	((utility or effective*) adj2 analys*).tw.	37800
18	(willing* adj2 pay*).tw.	14735
19	(EQ5D* or EQ-5D*).tw.	26137

Searches
20 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 5262
21 (european* adj2 quality adj3 ("5" or five)).tw. 996
22 or/4-21 635358
23 3 and 22 7788
24 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ 1716014
25 exp "organisation for economic co-operation and development"/ 2774
26 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ 3801223
27 european union/ 31487
28 developed country/ 35727
29 or/25-28 3834983
30 24 not 29 1561961
31 23 not 30 6971
32 limit 31 to english language 6647
33 (letter or editorial).pt. 2081948
34 32 not 33 6549
35 Case report/ 2939178
36 34 not 35 6182

Searches
37 nonhuman/ not human/ 5325269
38 36 not 37 6027
39 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5742113
40 38 not 39 4181
41 limit 40 to yr="2014 -Current" 2288
Note: in the re-run Line 41 was changed to limit 40 to dc=20231101-20241014.

Database name: International HTA Database

Searches
1 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*)[abs] AND (English)[Language] FROM 2014 TO 2023 15
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*)[Title] AND (English)[Language] FROM 2014 TO 2023 7
3 ("pneumonia"[mh] or "bronchopneumonia"[mh] or "pleuropneumonia"[mh] or "pneumonia bacterial"[mh] or "chlamydial pneumonia"[mh] or "pneumonia mycoplasma"[mh] or "pneumonia pneumococcal"[mh] or "pneumonia rickettsial"[mh] or "pneumonia staphylococcal"[mh] or "pneumonia necrotizing"[mh] or "pneumonia viral"[mh] or "organizing pneumonia"[mh] or "cryptogenic organizing pneumonia"[mh] or "healthcare-associated pneumonia"[mh]) AND (English)[Language] FROM 2014 TO 2023 21
4 1 OR 2 OR 3 30
Note: in the re-run the date was changed to FROM 2023 TO 2024.

Database name: MEDLINE ALL

Searches
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, rickettsial/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or cryptogenic organizing pneumonia/ or healthcare-associated pneumonia/ 125178
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 159311
3 1 or 2 229286
4 Cost-Benefit Analysis/ 93463
5 Quality-Adjusted Life Years/ 15940
6 Markov Chains/ 16047
7 exp Models, Economic/ 16244
8 cost*.ti. 146284
9 (cost* adj2 utilit*).tw. 7812
10 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw.279720
11 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 47585
12 (qualit* adj2 adjust* adj2 life*).tw. 18059
13 QALY*.tw. 14611
14 (incremental* adj2 cost*).tw. 17628

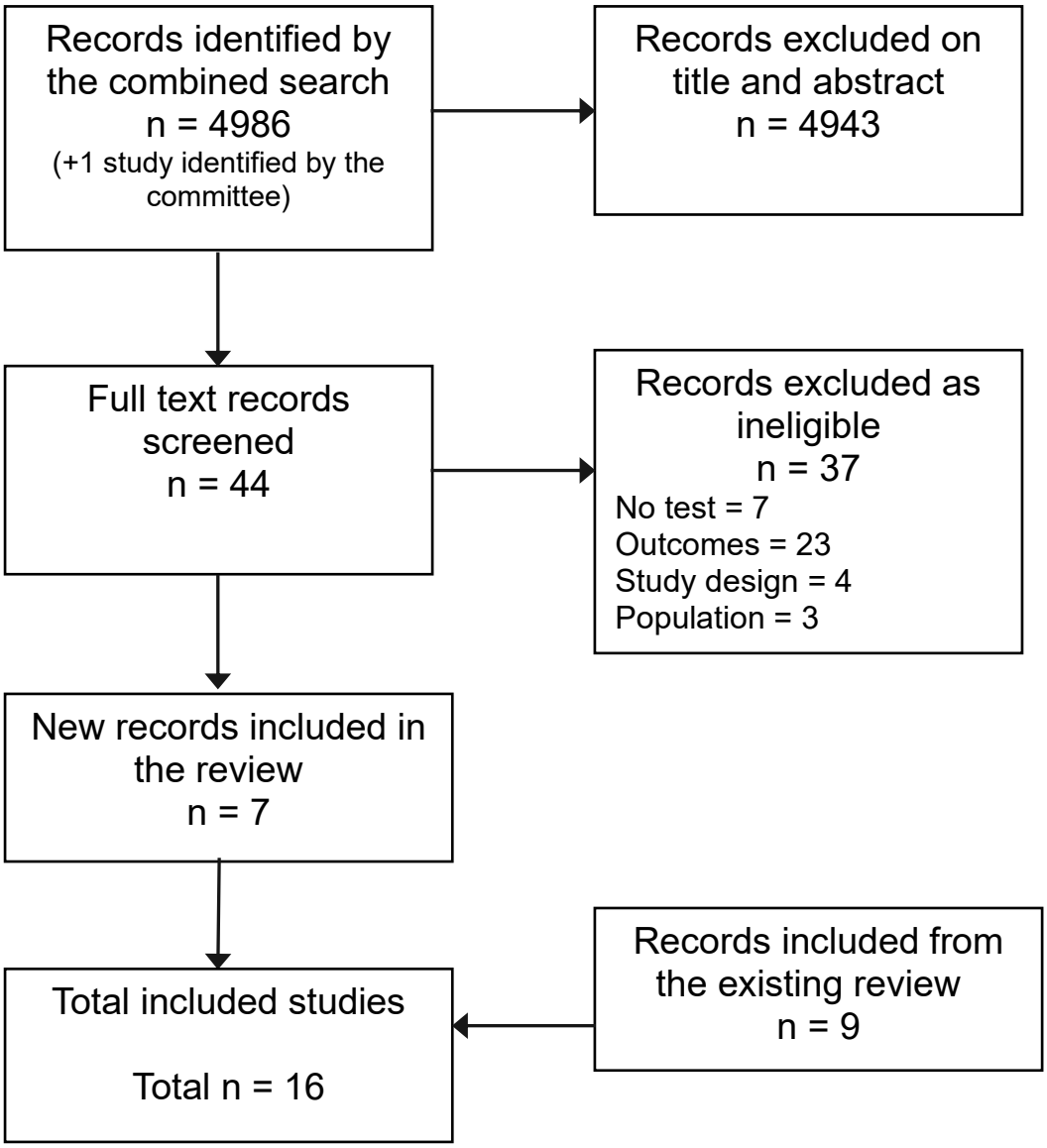
Searches	
15	ICER.tw. 6134
16	utilities.tw. 9537
17	markov*.tw. 32169
18	(dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. 54722
19	((utility or effective*) adj2 analys*).tw. 25292
20	(willing* adj2 pay*).tw. 9954
21	(EQ5D* or EQ-5D*).tw. 13646
22	((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 3930
23	(european* adj2 quality adj3 ("5" or five)).tw. 723
24	or/4-23 506237
25	3 and 24 3855
26	afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ 1312779
27	"organisation for economic co-operation and development"/ 565
28	australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ 3515662
29	european union/ 17814
30	developed countries/ 21444
31	or/27-30 3531767

Searches		
32	26 not 31	1222696
33	25 not 32	3418
34	limit 33 to english language	3185
35	limit 34 to (letter or historical article or comment or editorial or news or case reports)	181
36	34 not 35	3004
37	Animals/ not (Animals/ and Humans/)	5137547
38	36 not 37	2921
39	limit 38 to yr="2014 -Current"	1534
Note: in the re-run the following lines were used:		
38	36 not 37	
39	limit 38 to ed=20231101-20241014	
40	limit 38 to dt=20231101-20241014	
41	39 or 40	

Database name: NHS Economic Evaluation Database (NHS EED)

Searches
1 MeSH DESCRIPTOR Pneumonia 252
2 MeSH DESCRIPTOR bronchopneumonia 1
3 MeSH DESCRIPTOR pleuropneumonia 0
4 MeSH DESCRIPTOR pneumonia, bacterial 90
5 MeSH DESCRIPTOR chlamydial pneumonia 0
6 MeSH DESCRIPTOR pneumonia, mycoplasma 3
7 MeSH DESCRIPTOR pneumonia, pneumococcal 48
8 MeSH DESCRIPTOR pneumonia, rickettsial 0
9 MeSH DESCRIPTOR pneumonia, staphylococcal 10
10 MeSH DESCRIPTOR pneumonia, necrotizing 0
11 MeSH DESCRIPTOR pneumonia, viral 9
12 MeSH DESCRIPTOR Cryptogenic Organizing Pneumonia 0
13 MeSH DESCRIPTOR healthcare-associated pneumonia 0
14 (pneumonia) OR (pneumonias) 1118
15 (bronchopneumon*) OR (pleuropneumon*) 3
16 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 1120
17 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15) IN NHSEED 425
18 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15) IN NHSEED FROM 2014 TO 2024 11
Note: no re-run required as the database has been archived and not updated since 31 March 2015.

Appendix C – Effectiveness and prognostic evidence study selection



Appendix D – Effectiveness/ Prognostic evidence

Markussen, 2024

Bibliographic Reference	Markussen, Dagfinn L; Serigstad, Sondre; Ritz, Christian; Knoop, Siri T; Ebbesen, Marit H; Faurholt-Jepsen, Daniel; Heggelund, Lars; van Werkhoven, Cornelis H; Clark, Tristan W; Bjorneklett, Rune O; Kommedal, Oyvind; Ulvestad, Elling; Grewal, Harleen M S; Diagnostic Stewardship in Community-Acquired Pneumonia With Syndromic Molecular Testing: A Randomized Clinical Trial.; JAMA network open; 2024; vol. 7 (no. 3); e240830

Study details

Study type	Test and treat randomised controlled trial (RCT)
Study location	Norway
Study setting	The ED of Haukeland University Hospital, a large tertiary care hospital in Bergen, Norway.
Study dates	This parallel-arm, single-blinded, single-centre, randomized clinical superiority trial was conducted between September 25, 2020, and June 21, 2022,
Inclusion criteria	Patients were eligible for inclusion if they were 18 years or older; presented to the ED with suspected CAP; and met at least 2 of the following criteria: new or worsening cough, new or worsening expectoration, new or worsening dyspnoea, haemoptysis, pleuritic chest pain, radiological evidence of pneumonia, abnormalities on chest auscultation and/or percussion, or fever (38.0 °C).
Exclusion criteria	Patients were ineligible if they had cystic fibrosis, had severe bronchiectasis, were hospitalized within the past 14 days prior to admission, were under a palliative approach (ie, life expectancy of <2 weeks), or were not willing to provide an LRT sample
Intervention(s)	Patients randomized to the intervention arm received rapid syndromic PCR testing (BioFire FilmArray Pneumonia plus Panel; bioMérieux) of LRT samples and standard of care
Comparator	Patients randomized to the standard-of-care arm received standard microbiological diagnostics alone.
Outcome measures	Two primary outcomes were the (1) provision of pathogen-directed treatment based on a relevant microbiological test result and (2) time to provision of pathogen-directed treatment (within 48 hours after randomization). The first was a binary outcome, whereas the second was an event-time outcome wherein right censoring was present (ie, patients may cease participation due to death, discharge, or reaching 48 hours after randomization without receiving pathogen-directed treatment). Primary outcomes were defined for all patients who were randomized.
Number of participants	A total of 2265 patients were assessed for eligibility, of whom 374 participated, with 187 patients randomized to each arm. Patients

	included 153 females (40.9%) and 221 males (59.1%), with a median (IQR) age of 72 (60-79) years. Among these patients, 208 had a diagnosis of CAP, of whom 200 (97 in the intervention arm and 103 in the standard-of-care arm) provided an LRT sample.
Methods of analysis	Because 2 primary outcomes were used, separate sample size calculations were performed for each outcome at a 2-sided significance level of .05/2 = .025 (instead of .05), assuming a power of 80%. To detect an increase in the provision of pathogen-directed treatment from .40 to .50, the sample size was required to be 470 per arm. Similarly, to detect a reduction of 0.2 SD in the time to provision of pathogen-directed treatment, it was established the sample size to be 477 per arm (ie, 954 in total). Allowing for a 10% dropout rate resulted in a total sample size of 1060 patients. The 2 primary outcomes were analysed according to the intention-to-treat principle, and Bonferroni adjustment was applied. Available-case analyses were used for the secondary outcomes. For binary outcomes, logistic regression models with logit and identity link functions were used to estimate odds ratios (ORs) and absolute risk differences, respectively. Two models were fitted for the event-time primary outcome: Cox proportional hazards regression model and restricted mean survival time model.16 The proportional hazards assumption for the Cox regression model was assessed visually using cumulative log-log plots. The restricted mean survival time model is a flexible survival analysis model that does not require proportional hazards because it is based on survival curves, which may be estimated parametrically or nonparametrically.17 Kaplan-Meier survival curves and log-rank tests were also reported. For the 2 primary outcomes, a post hoc analysis that was adjusted for season was also carried out through inclusion of an indicator of whether recruitment took place from September 25, 2020, to June 1, 2021, or from August 15, 2021, to June 21, 2022.
Additional comments	the study included a mixture of patients from intensive care units with hospital-acquired pneumonia, ventilator-associated pneumonia, and CAP; thus, the findings may not be specifically applicable to patients with CAP.

Study arms

Intervention (N = 187)

Patients randomized to the intervention arm received rapid syndromic PCR testing (BioFire FilmArray Pneumonia plus Panel; bioMérieux) of LRT samples and standard of care

Control (N = 187)

Patients randomized to the standard-of-care arm received standard microbiological diagnostics alone.

Critical appraisal – Cochrane ROB 2.0 Checklist

Overall risk of bias	Moderate	The trial was stopped early for efficacy, and there could be a risk of inflated estimates of differences between the intervention and standard of care, although this risk could be small significant differences were found
Applicability as a source of data	Directly applicable	

Abelenda-Alonso, 2022

Bibliographic Reference	Abelenda-Alonso, Gabriela; Rombauts, Alexander; Gudiol, Carlota; Garcia-Lerma, Esther; Pallares, Natalia; Ardanuy, Carmen; Calatayud, Laura; Niubo, Jordi; Tebe, Cristian; Carratala, Jordi; Effect of positive microbiological testing on antibiotic de-escalation and outcomes in community-acquired pneumonia: a propensity score analysis.; Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases; 2022; vol. 28 (no. 12); 1602-1608

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location Spain Study setting Bellvitge University Hospital, a 700-bed public hospital in Barcelona, Spain. Study dates: January 1995 to February 2017
Inclusion criteria	All immunocompetent patients over the age of 18, admitted to the hospital with radiologically proven CAP via the emergency department, were included.
Exclusion criteria	Patients who died within 72 hours of hospital admission, those with an already targeted antimicrobial treatment as described below, and cases lacking data on de-escalation were excluded. Patients with empyema or aspiration CAP were also excluded.
Number of participants and	3677

recruitment methods	
Length of follow-up	Thirty-day case-fatality rate was defined as death due to any cause in the first 30 days of hospitalisation. Duration of antimicrobial IV therapy was considered from the day of the first IV antimicrobial dose to the last. Total duration of antimicrobial therapy was considered from the first day of antimicrobial treatment to the last, including all antimicrobial treatment received after hospital discharge. Adverse events were documented according to Medical Dictionary for Regulatory Activities (MedDRA) definitions. Length of hospital stay was measured from admission to emergency department until hospital discharge. CAP recurrence was defined as re-admission or consultation for persistence or clinical recurrence of the same clinical process of the first episode of CAP within 30 days of hospital discharge
Loss to follow up	A total of 3677 consecutive episodes of CAP were analysed. Microbiological results were positive in 1924 (52.3%) and nonpositive in 1753 (47.7%).
Outcome(s) of interest	The primary outcome was antimicrobial de-escalation. The secondary outcomes were 30-day case-fatality rate, duration of antimicrobial intravenous (IV) therapy, total duration of antimicrobial therapy, adverse events, length of hospital stay, and CAP recurrence.
Covariates adjusted for in the multivariable regression modelling	Adjustment for confounders was performed by inverse probability weighting propensity score, logistic regression, and cause-specific Cox model.
Additional comments	During the study period, because of the lack of a specific hospital policy, antimicrobial de-escalation was determined by the attending physicians in each case. The microbiological data and the antimicrobial de-escalation process in all study patients were assessed by at least two experienced clinical investigators who were blinded to the patient's outcomes.

Study arms

Positive (N = 1924)

Positive microbiological result

Non-positive (N = 1753)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 3677)
% Female No of events	n = 1182 ; % = 32.1

Characteristic	Study (N = 3677)
Age Median (IQR)	59 (56 to 78)

Critical appraisal – Cochrane ROB 2.0 Checklist

Overall risk of bias	Moderate	Due to retrospective study design and lack of control for possible selection bias
Applicability as a source of data	Directly applicable	

Capelastegui, 2014

Bibliographic Reference	Capelastegui, Alberto; Zalacain, Rafael; Bilbao, Amaia; Egurrola, Mikel; Iturriaga, Luis Alberto Ruiz; Quintana, Jose M; Gomez, Ainhoa; Esteban, Cristobal; Espana, Pedro P; Pneumococcal pneumonia: differences according to blood culture results.; BMC pulmonary medicine; 2014; vol. 14; 128

Study Characteristics

Study design	Prospective cohort study
Study details	Study location Two hospitals in northern Spain Study setting Cases diagnosed with pneumococcal pneumonia were selected from a cohort of hospitalized patients with pneumonia. Data were collected prospectively from two hospitals (Galdakao-Usansolo Hospital and Cruces University Hospital) in the Basque Country (northern Spain). GaldakaoUsansolo Hospital is a 400-bed general teaching hospital serving a population of 300,000, while Cruces University Hospital is a nearby large teaching hospital with a catchment population of 400,000. Study dates between January 2001 and July 2009.
Inclusion criteria	All patients with a diagnosis of pneumonia and at least one positive blood culture for Streptococcus pneumoniae taken within 48 hours of presentation to the hospital were included in the “pneumococcal bacteremic” group. The “pneumococcal non-bacteremic” group

	included patients with positive Streptococcus pneumoniae antigen in urine and negative blood cultures .
Exclusion criteria	Any individuals with concurrent meningitis and/or endocarditis were excluded from the analysis
Number of participants and recruitment methods	Patients selected were diagnosed with pneumococcal pneumonia and compared the subgroups in this sample with bacteremic and non-bacteremic pneumonia. A total of 891 patients were identified in the study period with a diagnosis of pneumococcal pneumonia and with blood culture results. Pneumococcal bacteremia was identified in 399 (44.8%) cases. The group of pneumococcal non-bacteremic pneumonia included 492 (55.2%) cases, all of them with positive antigen in urine and negative blood culture
Outcome(s) of interest	Clinical in-hospital measures included: whether the patient 1) was admitted to the intensive care unit (ICU); 2) received mechanical ventilation; or 3) developed septic shock; as well as whether there was 4) treatment failure; or 5) severe sepsis. Outcome measures included: 1) in-hospital mortality; 2) and 3) mortality at 15 and 30 days after admission; 4) hospital readmission within 30 days; and 5) length of hospital stay (calculated as the date of discharge minus the date of admission).
Covariates adjusted for in the multivariable regression modelling	Univariate logistic regression models were used to compare in-hospital course and outcomes between the two groups of patients (unadjusted results). Then, multivariate logistic regression models were built for the comparison, adjusting for severity of illness at admission, measured by CURB-65, as well as for patient characteristics and variables related to the process of care found to be significantly different in the groups stratified by blood culture results. In the final multivariate models, only adjusting variables found to be statistically significant were kept.

Study arms

Intervention (N = 492)
patients with negative blood culture

Control (N = 399)
patients with positive culture results

Population characteristics

Arm-level characteristics

Characteristic	Intervention (N = 492)	Control (N = 399)
Age (years) Mean (SD)	63.6 (18.5)	65.2 (17)
1 comorbid condition No of events	n = 130 ; % = 32.6	n = 156 ; % = 31.7

Critical appraisal – Cochrane ROB 2.0 Checklist

Overall risk of bias	Moderate	Due to of information on missing outcome data
Applicability as a source of data	Directly applicable	

Cilloniz, 2017

Bibliographic Reference	Cilloniz, Catia; Ceccato, Adrian; de la Calle, Cristina; Gabarrus, Albert; Garcia-Vidal, Carolina; Almela, Manel; Soriano, Alex; Martinez, Jose Antonio; Marco, Francesc; Vila, Jordi; Torres, Antoni; Time to blood culture positivity as a predictor of clinical outcomes and severity in adults with bacteremic pneumococcal pneumonia.; PloS one; 2017; vol. 12 (no. 8); e0182436

Study Characteristics

Study design	Prospective cohort study
Study details	Study location Prospective observational study carried out in 278 hospitalized adult CAP patients with positive blood culture for *Streptococcus pneumonia* (2003–2015). Study setting A prospective observational study including all adults consecutively admitted between 2003 to 2015 with a diagnosis of community-acquired pneumococcal pneumonia to the Hospital Clinic of Barcelona, Spain, an 800-bed third-level hospital covering an urban population of 540,000 inhabitants. Study dates 2003–2015
Exclusion criteria	Authors excluded patients who were immunosuppressed, receiving immunosuppressant (those taking >10 mg/day of prednisone or cytotoxic therapy) and all patients known to have human immunodeficiency virus infection
Number of participants and recruitment methods	A total of 278 cases of bacteremic pneumococcal pneumonia were analysed

Loss to follow up	During the study period, 4,639 patients were admitted in the Emergency Department with the diagnosis of CAP. Blood cultures were performed on 3,274 (71%) and were positive in 419 (13%). Of these, 301 (72%) were positive for *S. pneumoniae*, and 23 were excluded from the analysis due to missing TTP, to having human immunodeficiency virus infection and/or who were receiving immunosuppressant. Therefore, 278 cases were finally included in the study.
Outcome(s) of interest	The primary outcome was in-hospital mortality. Secondary outcomes included length of hospital stay, 30-day mortality, ICU admission, length of stay in ICU, ICU mortality, and need of mechanical ventilation.
Covariates adjusted for in the multivariable regression modelling	Regression analyses were used to examine the associations between outcomes (a linear regression analysis for length of hospital stay, two logistic regression analyses for in-hospital mortality and 30-day mortality, and a multinomial logistic regression analysis for non-invasive or invasive mechanical ventilation) and risk factors. In a first step, each risk factor was tested individually. In a second step, all risk factors which showed an association in the univariate model ($p<0.10$) were added into the multivariate model. Finally, a backward stepwise selection ($pin<0.05$, $pout<0.10$) was used to determine factors associated with outcome. The beta coefficient (β) and 95% confidence interval (CI) and the odds ratio (OR) and 95% (CI) were calculated where applicable. The Hosmer-Lemeshow goodness-of-fit test was performed to assess the overall fit of the logistic regression models, the R2 for the linear regression model, and the Cox and Snell R2 and the Nagelkerke R2 for the multinomial logistic regression model. Internal validation of the prediction models was conducted using ordinary nonparametric bootstrapping with 1,000 bootstrap samples and bias-corrected, accelerated 95% CIs [22]. The area under the ROC curve of the multivariate models to predict in-hospital mortality, 30-day mortality, non-invasive and invasive mechanical ventilation were calculated. Simple imputations of random effects were used, if necessary, for variables with missing values.
Additional comments	Patients were stratified into risk classes using the validated prediction rule calculated according to the Pneumonia Severity Index (PSI) score. Authors also calculated the CURB-65 and the sequential organ failure assessment (SOFA) scores at admission. Empirical antibiotic treatment was administered according to the Infectious Disease Society of America/American Thoracic Society (IDSA/ATS) guidelines for management of CAP. All surviving patients were visited at 30–40 days after discharge.

Study arms

Intervention early detection <9.2h (N = 69)

Time to positivity of blood culture (TTP)

Intervention late detection 9.2h (N = 209)

Population characteristics

Arm-level characteristics

Characteristic	Intervention early detection <9.2h (N = 69)	Intervention late detection 9.2h (N = 209)
Age median (IQR) Median (IQR)	67 (50 to 81)	60 (46 to 75)
Male n (%) Sample size	n = 39 ; % = 57	n = 126 ; % = 60
Comorbidity, n (%) Sample size	n = 37 ; % = 54	n = 126 ; % = 60

Critical appraisal – Cochrane ROB 2.0 Checklist

Overall risk of bias	Moderate	Due to lack of information on adjustments for confounders
Applicability as a source of data	Directly applicable	

Lee, 2020

Bibliographic Reference	Lee, Jonghoo; Song, Jae-Uk; Performance of pneumococcal urinary antigen test in patients with community-onset pneumonia: a propensity score-matching study.; The Korean journal of internal medicine; 2020; vol. 35 (no. 3); 630-640

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location Korea Study setting Hospitalised adult patients Study dates

	Adult patients (aged ≥ 18 years) who were hospitalized with pneumonia between January 2012 and December 2015 were investigated
Exclusion criteria	We excluded the following types of patients: (1) those who were readmitted due to pneumonia within 10 days of leaving the hospital; (2) those who were transferred from other hospitals after hospitalization for > 48 hours; (3) those with obstructive pneumonia; (4) those who had immunocompromised status, such as neutropenia (absolute neutrophil count < 1,500 cells/μL) after chemotherapy or human immunodeficiency virus infection; (5) those who did not receive guideline-concordant antibiotic therapy; and (6) those who had hospital-acquired pneumonia (HAP).
Number of participants and recruitment methods	1257 eligible Patients were identified by the use of the international diagnostic codes version 10 to screen for possible cases as follows: J18.0 to 18.9 as representative codes of pneumonia in the primary discharge diagnosis
Loss to follow up	1966 were assessed for eligibility 588 were excluded for various reasons 1257 were eligible
Outcome(s) of interest	30-day mortality
Covariates adjusted for in the multivariable regression modelling	The propensity score was calculated by logistic regression analysis using the covariates of baseline characteristics. Standardized differences were estimated for all baseline covariates before and after matching to assess prematch imbalance and postmatch balance.

Study arms

Positive PUAT (N = 163)
Positive PUAT of the entire cohort (n=1257)

Negative PUAT (N = 1094)
Negative PUAT of the entire cohort (n=1257)

Population characteristics

Arm-level characteristics

Characteristic	Positive PUAT (N = 163)	Negative PUAT (N = 1094)
Age (years)	73 (66 to 81)	72 (61 to 80)

Characteristic	Positive PUAT (N = 163)	Negative PUAT (N = 1094)
Median (IQR)		
Male sex Sample size	n = 105 ; % = 64.4	n = 673 ; % = 61.5
PSI score Median (IQR)	98 (76 to 123)	92 (70 to 121)

Shen, 2011

Bibliographic Reference	Shen, Ching-Fen; Wang, Shih-Min; Liu, Ching-Chuan; A new urinary antigen test score correlates with severity of pneumococcal pneumonia in children.; Journal of the Formosan Medical Association = Taiwan yi zhi; 2011; vol. 110 (no. 10); 613-8

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location Taiwan Study setting children with pneumococcal pneumonia who were hospitalized at the National Cheng Kung University Hospital Study dates Children diagnosed by positive urinary pneumococcal antigen test at the National Cheng Kung University Hospital from 2002 through 2007
Number of participants and recruitment methods	119 children hospitalized with pneumonia diagnosed by positive urinary pneumococcal antigen test
Loss to follow up	NR
Outcome(s) of interest	ICU stay Oxygen requirement Intubation (mechanical ventilation)

	Mortality
Covariates adjusted for in the multivariable regression modelling	NR

Study arms

Group 1 (N = 40)

Group 2 (N = 44)

Group 3 (N = 35)

Critical appraisal – Cochrane ROB 2.0 Checklist

Overall risk of bias	Moderate	Due to retrospective design and possible selection bias, although this was minimised by adjustments for confounders.
Applicability as a source of data	Directly applicable	

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Study details

Trial registration number and/or trial name	NCT05937126)
Study type	test and treat randomised controlled trial (RCT)
Study location	USA
Study setting	Single-centre trial conducted at the Mayo Clinic Rochester, USA.
Study dates	Recruitment occurred between September 15, 2020, and September 19, 2022. No further information provided.
Sources of funding	Funding was received from the following sources: - bioMérieux - Moderna
Inclusion criteria	Inclusion criteria Participants were included if they were aged 18 years or over with suspected pneumonia and admitted to the Mayo Clinic Hospital, and respiratory samples meeting study enrolment criteria

	(expectorated or induced sputum, tracheal secretions, or bronchoalveolar lavage fluid culture).
Exclusion criteria	Exclusion criteria Patients were excluded if they were younger than 18 years, had specimens with poor quality Gram stain for expectorated sputum culture or had positive respiratory cultures in the 7 days before the study, had previously enrolled in the study, had not provided Minnesota research authorisation, or were affected by the Global Data Protection.
Intervention(s)	BioFire FilmArray pneumonia panel plus conventional culture and AST (antimicrobial susceptibility testing). BioFire FilmArray panel was performed 24h per day for 7 days per week as per instructions and results reported in the EHR (electronic health record). Viruses *egionella pneumophila, Chlamydia pneumoniae*, and *Mycoplasma pneumoniae* were reported as either present or absent while other bacteria was reported in quantity.
Comparator	Conventional culture and AST (antimicrobial susceptibility testing). Antimicrobial stewardship review included assessments and recommendations for antibiotic modifications based on the clinical data.
Outcome measures	Outcomes • Mortality within 30 days • Length of stay in hospital • Length of stay in the ICU • Need for ventilators
Number of participants	Randomly assigned specimen: N=1181 Intervention: n= 582 (19 excluded: 1 outpatient, 1 over accrual, 9 product recalls, 8 sample errors) Control: n=599 (10 excluded: 7 outpatients, 2 over accrual, 1 sample error)
Duration of follow-up	
Methods of analysis	Modified intention-to-treat population was used to evaluate the effect of the BioFire FilmArray pneumonia panel (Participants with community-acquired, hospital-acquired, or ventilator-associated pneumonia were analysed separately)

Study arms

BioFire FilmArray pneumonia panel plus conventional culture and AST (N = 563)

Conventional culture and AST (N = 589)

Characteristics

Study-level characteristics

Characteristic	Study (N = 1152)
% Female Nominal	36.4
Mean age (SD) Mean (range)	62.3 (54-74)
Comorbidities - Diabetes with or without end-organ damage Sample size	n = 331 ; % = 28.7
Comorbidities - Myocardial infarction Sample size	n = 129 ; % = 11.2
Comorbidities - Congestive heart failure Sample size	n = 247 ; % = 21.4
Comorbidities - Dementia Sample size	n = 6 ; % = 0.5
Comorbidities - Renal disease Sample size	n = 245 ; % = 21.3
Comorbidities - COPD Sample size	n = 194 ; % = 16.8
Comorbidities - Any solid tumour in previous 5 years with or without metastasis Sample size	n = 203 ; % = 17.6
Comorbidities - Leukaemia or lymphoma Sample size	n = 138 ; % = 12
Comorbidities - Any liver disease (mild, moderate, or severe) Sample size	n = 41 ; % = 3.6

Characteristic	Study (N = 1152)
Comorbidities - HIV or AIDS Sample size	n = 5 ; % = 0.4
Comorbidities - Solid organ transplant Sample size	n = 83 ; % = 7.2
Comorbidities - Bone marrow transplant Sample size	n = 47 ; % = 4.1

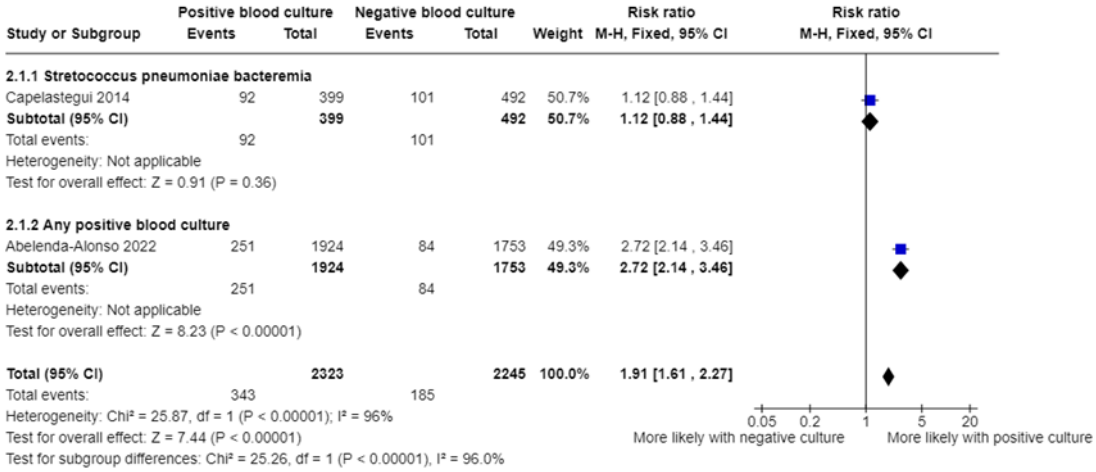
Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E – Forest plots

Blood culture in adults

Admission to ITU:



Rapid syndromic PCR testing compared to standard care in adults

Mortality within 30 days

Re-admission to hospital within 30 days

Admission to ICU at 96 hours

Admission to ICU at 30 days

Change in antibiotics

Appendix F – GRADE tables

Table 8 Positive blood culture compared to negative blood culture for making care decisions in adults

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive blood culture	negative blood culture	Relative (95% CI)	Absolute (95% CI)	
Admission to ITU - Stretococcus pneumoniae bacteremia											
1	non-randomised studies	not serious	serious[a]	not serious	serious[b]	none	92/399 (23.1%)	101/492 (20.5%)	**RR 1.12** (0.88 to 1.44)	**25 more per 1,000** (from 25 fewer to 90 more)	⊕◯◯◯ Very low
Admission to ITU - Any positive blood culture											
1	non-randomised studies	not serious	serious[a]	not serious	not serious	none	251/1924 (13.0%)	84/1753 (4.8%)	**RR 2.72** (2.14 to 3.46)	**82 more per 1,000** (from 55 more to 118 more)	⊕◯◯◯ Very low
Need for mechanical ventilation (Stretococcus pneumoniae bacteremia)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive blood culture	negative blood culture	Relative (95% CI)	Absolute (95% CI)	
1	non-randomised studies	not serious	serious[a]	not serious	serious[b]	none	42/399 (10.5%)	27/492 (5.5%)	**RR 1.92** (1.20 to 3.05)	**50 more per 1,000** (from 11 more to 112 more)	⊕◯◯◯ Very low
Treatment failure (Stretococcus pneumoniae bacteremia)											
1	non-randomised studies	not serious	serious[a]	not serious	serious[b]	none	72/399 (18.0%)	59/492 (12.0%)	**RR 1.50** (1.10 to 2.07)	**60 more per 1,000** (from 12 more to 128 more)	⊕◯◯◯ Very low
In hospital mortality (Stretococcus pneumoniae bacteremia)											
1	non-randomised studies	not serious	serious[a]	not serious	serious[b]	none	35/399 (8.8%)	22/492 (4.5%)	**RR 1.96** (1.17 to 3.29)	**43 more per 1,000** (from 8 more to 102 more)	⊕◯◯◯ Very low
30-day mortality (Stretococcus pneumoniae bacteremia)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive blood culture	negative blood culture	Relative (95% CI)	Absolute (95% CI)	
1	non-randomised studies	not serious	serious[a]	not serious	not serious		37/399 (9.3%)	18/492 (3.7%)	**RR 2.53** (1.47 to 4.38)	**56 more per 1,000** (from 17 more to 124 more)	-
30-day readmission (Stretococcus pneumoniae bacteremia)											
1	non-randomised studies	not serious	serious[a]	not serious	serious[c]	none	10/399 (2.5%)	27/492 (5.5%)	**RR 0.46** (0.22 to 0.93)	**30 fewer per 1,000** (from 43 fewer to 4 fewer)	⨁◯◯◯ Very low
Hospital stay <3 days (Stretococcus pneumoniae bacteremia)											
1	non-randomised studies	not serious	serious[a]	not serious	not serious	none	295/399 (73.9%)	373/492 (75.8%)	**RR 0.98** (0.90 to 1.05)	**15 fewer per 1,000** (from 76 fewer to 38 more)	⨁◯◯◯ Very low
Length of hospital stay (Stretococcus pneumoniae bacteremia) [MID 2.75)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive blood culture	negative blood culture	Relative (95% CI)	Absolute (95% CI)	
1	non-randomised studies	not serious	serious[a]	not serious	serious[d]	none	399	492	-	MD **3 days more** (1.57 more to 4.43 more)	⨁◯◯◯ Very low
Antimicrobial de-escalation (any positive blood culture)											
1	non-randomised studies	serious[e]	serious[a]	not serious	not serious	none	648/1924 (33.7%)	179/1753 (10.2%)	**RR 3.30** (2.83 to 3.84)	**235 more per 1,000** (from 187 more to 290 more)	⨁◯◯◯ Very low

CI=confidence interval; MD=mean difference; ITU= intensive therapy unit; RR=risk ratio;
a. Downgraded once as single study
b. Downgraded once as 95% CI crosses one clinical decision threshold (1.25)
c. Downgraded once as 95% CI crosses one clinical decision threshold (0.8)
d. Downgraded once as 95% CI crosses one clinical decision threshold (2.75)
e. Downgraded once for moderate risk of bias

Table 9 Early blood culture positivity compared to late blood culture positivity for planning care in streptococcus pneumoniae bacteraemia in adults

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	early blood culture positivity	late blood culture positivity	Relative (95% CI)	Absolute (95% CI)	
Length of stay <= 9 days											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	47/69 (68.1%)	92/209 (44.0%)	**RR 1.55** (1.24 to 1.93)	**242 more per 1,000** (from 106 more to 409 more)	⨁◯◯◯ Very low
In hospital mortality											
1	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	10/69 (14.5%)	9/209 (4.3%)	**RR 3.37** (1.43 to 7.94)	**102 more per 1,000** (from 19 more to 299 more)	⨁◯◯◯ Very low
30-day mortality											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	10/69 (14.5%)	11/209 (5.3%)	**RR 2.75** (1.22 to 6.20)	**92 more per 1,000** (from 12 more to 274 more)	⨁◯◯◯ Very low
ICU admission											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	27/69 (39.1%)	60/209 (28.7%)	**RR 1.36** (0.95 to 1.96)	**103 more per 1,000** (from 14 fewer to 276 more)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	early blood culture positivity	late blood culture positivity	Relative (95% CI)	Absolute (95% CI)	
ICU mortality											
1	non-randomised studies	serious[a]	serious[b]	not serious	very serious[d]	none	4/69 (5.8%)	4/209 (1.9%)	**RR 3.03** (0.78 to 11.79)	**39 more per 1,000** (from 4 fewer to 207 more)	⨁◯◯◯ Very low
Need for mechanical ventilation											
1	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	11/69 (15.9%)	11/209 (5.3%)	**RR 3.03** (1.37 to 6.68)	**107 more per 1,000** (from 19 more to 299 more)	⨁◯◯◯ Very low

CI=confidence interval; ICU=intensive care unit; RR=risk ratio
a. Downgraded once for moderate risk of bias
b. Downgraded once for single study
c. Downgraded once as CI crosses one clinical threshold (1.25)
d. Downgraded twice as CI crosses two clinical threshold (0.8-1.25)

Table 10 Positive rapid syndromic PCR testing of lower respiratory tract samples compared to negative testing for determining care in adults

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive rapid syndromic PCR testing of lower respiratory tract samples	negative testing	Relative (95% CI)	Absolute (95% CI)	
Pathogen directed treatment based on test result within 48 h (CAP pts only)											

Certainty assessment							№ of patients		Effect		Certainty	
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive rapid syndromic PCR testing of lower respiratory tract samples	negative testing	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[a]	serious[b]	not serious	not serious	none	46/97 (47.4%)	16/103 (15.5%)	**RR 3.05** (1.86 to 5.02)	**318 more per 1,000** (from 134 more to 624 more)	⨁⨁◯◯ Low	
Readmission (CAP pts only)												
1	randomised trials	serious[a]	serious[b]	not serious	very serious[c]	none	14/97 (14.4%)	19/103 (18.4%)	**RR 0.75** (0.35 to 1.59)	**46 fewer per 1,000** (from 120 fewer to 109 more)	⨁◯◯◯ Very low	
30-day mortality (CAP pts only)												
1	randomised trials	serious[a]	serious[b]	not serious	very serious[c]	none	3/97 (3.1%)	4/103 (3.9%)	**RR 0.79** (0.17 to 3.62)	**8 fewer per 1,000** (from 32 fewer to 102 more)	⨁◯◯◯ Very low	
Length of stay												
1	randomised trials	serious[a]	serious[b]	not serious	not serious	none	97	103	-	median **0.1 days fewer** (0 to 0)	⨁⨁◯◯ Low	

CAP=community acquired pneumonia; CI=confidence interval; PCR=polymerase chain reaction; RR=risk ratio
a. Downgraded once as study at moderate risk of bias
b. Downgraded once as single study
c. Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)

Table 11 Rapid syndromic PCR testing compared to standard care in adults

Certainty assessment							Effect	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	
Mortality within 30 days								
1	randomised trials	not serious	serious[a]	not serious	serious[c]	none	RR 0.79 (0.58 to 1.07)	⊕⊕◯◯ Low
Re-admission to hospital within 30 days								
1	randomised trials	not serious	serious[a]	not serious	serious[c]	none	RR 0.77 (0.51 to 1.16)	⊕◯◯◯ Very low
Admission to ICU at 96 hours								
1	randomised trials	not serious	serious[a]	not serious	not serious	none	0.39 (0.17 to 0.86)	⊕◯◯◯ Moderate
Admission to ICU at 30 days								
1	randomised trials	not serious	serious[a]	not serious	Very serious[b]	none	RR 0.61 (0.21 to 1.75)	⊕⊕◯◯ Very low
Change in antibiotics								
1	randomised trials	not serious	serious[a]	not serious	not serious	none	RR 0.89 (0.81 to 0.98)	⊕◯◯◯ Moderate

CI=confidence interval; ICU=intensive care unit; RR=risk ratio
a. Downgraded once as single study
b. Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
c. Downgraded once as CI crosses one clinical threshold (0.8 or 1.25)

Table 12 Positive pneumococcal urinary antigen test (PUAT) compared to negative PUAT for determining care in adults

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive pneumococcal urinary antigen test (PUAT)	negative PUAT	Relative (95% CI)	Absolute (95% CI)	
Length of hospital stay - Full cohort [MID: 4.4]											
1	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	163	1094	-	MD **1.2 days more** (0.71 fewer to 3.11 more)	⨁◯◯◯ Very low
Length of hospital stay - Propensity score matched [MID: 5.25]											
1	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	161	161	-	MD **1.4 days fewer** (3.87 fewer to 1.07 more)	⨁◯◯◯ Very low
Duration of antibiotic therapy - Full cohort [MID: 4.1]											
1	non-randomised studies	serious[b]	serious[b]	not serious	not serious	none	163	1094	-	MD **0.5 days fewer** (1.54 fewer to 0.54 more)	⨁◯◯◯ Very low
Duration of antibiotic therapy - Propensity score matched [3.35]											
1	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	161	161	-	MD **0.8 days fewer** (2.19 fewer to 0.59 more)	⨁◯◯◯ Very low

CI=confidence interval; MD=mean difference; MID=minimal important difference; PUAT=pneumococcal urinary antigen test
a. Downgraded once for moderate risk of bias

b. Downgraded once for single study

Table 13 Positive pneumococcal urinary antigen test (PUAT) compared to negative PUAT for determining care in children

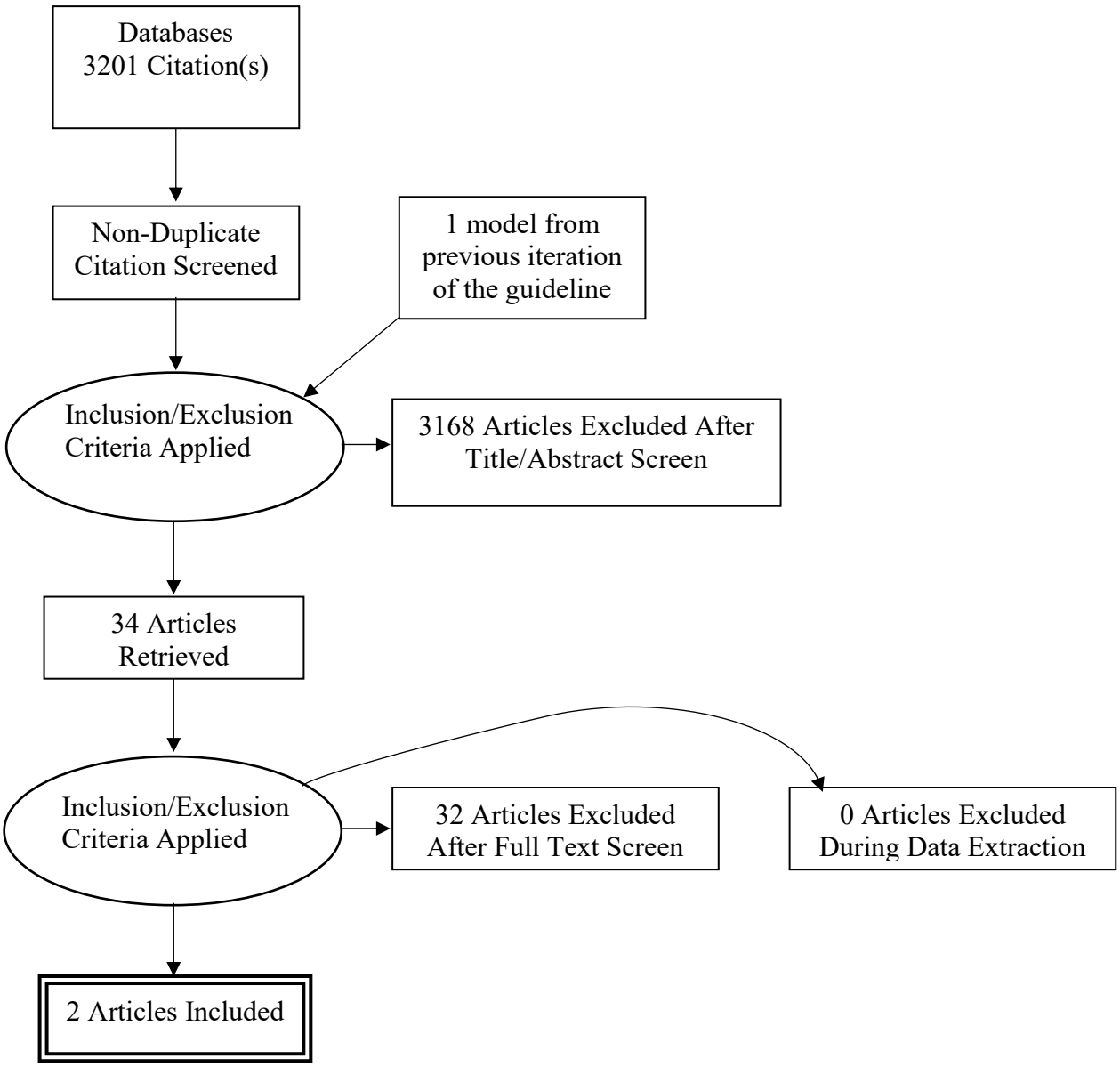
Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive pneumococcal urinary antigen test (PUAT)	negative PUAT	Relative (95% CI)	Absolute (95% CI)	
Antigen reactivity score 8 vs. score 5-7 - Admission to ITU											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	30/40 (75.0%)	21/44 (47.7%)	**RR 1.57** (1.10 to 2.25)	**272 more per 1,000** (from 48 more to 597 more)	⨁◯◯◯ Very low
Antigen reactivity score 8 vs. score 5-7 - Require oxygen therapy											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	26/40 (65.0%)	15/44 (34.1%)	**RR 1.91** (1.19 to 3.05)	**310 more per 1,000** (from 65 more to 699 more)	⨁◯◯◯ Very low
Antigen reactivity score 8 vs. score 5-7 - Invasive mechanical ventilation											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	8/40 (20.0%)	1/44 (2.3%)	**RR 8.80** (1.15 to 67.29)	**177 more per 1,000** (from 3 more to 1,000 more)	⨁◯◯◯ Very low
Antigen reactivity score 8 vs. score 5-7 - Mortality											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	1/40 (2.5%)	0/44 (0.0%)	**RR 3.29** (0.14 to 78.59)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive pneumococcal urinary antigen test (PUAT)	negative PUAT	Relative (95% CI)	Absolute (95% CI)	
Antigen reactivity score 8 vs. score 2-4 - Admission to ITU											
1	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	30/40 (75.0%)	10/35 (28.6%)	**RR 2.63** (1.51 to 4.57)	**466 more per 1,000** (from 146 more to 1,000 more)	⨁◯◯◯ Very low
Antigen reactivity score 8 vs. score 2-4 - Require oxygen therapy											
1	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	26/40 (65.0%)	5/35 (14.3%)	**RR 4.55** (1.96 to 10.57)	**507 more per 1,000** (from 137 more to 1,000 more)	⨁◯◯◯ Very low
Antigen reactivity score 8 vs. score 2-4 - Invasive mechanical ventilation											
1	non-randomised studies	serious[a]	serious[b]	not serious	very serious[d]	none	8/40 (20.0%)	2/35 (5.7%)	**RR 3.5** (0.8 to 15.4)	**143 more per 1,000** (from 11 fewer to 823 more)	⨁◯◯◯ Very low
Antigen reactivity score 8 vs. score 2-4 - Mortality											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	1/40 (2.5%)	1/35 (2.9%)	**RR 0.88** (0.06 to 13.48)	**3 fewer per 1,000** (from 27 fewer to 357 more)	⨁◯◯◯ Very low
Antigen reactivity score 5-7 vs. score 2-4 - Admission to ITU											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	positive pneumococcal urinary antigen test (PUAT)	negative PUAT	Relative (95% CI)	Absolute (95% CI)	
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	21/44 (47.7%)	10/35 (28.6%)	**RR 1.67** (0.91 to 3.07)	**191 more per 1,000** (from 26 fewer to 591 more)	⨁◯◯◯ Very low
Antigen reactivity score 5-7 vs. score 2-4 - Require oxygen therapy											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	15/44 (34.1%)	5/35 (14.3%)	**RR 2.39** (0.96 to 5.93)	**199 more per 1,000** (from 6 fewer to 704 more)	⨁◯◯◯ Very low
Antigen reactivity score 5-7 vs. score 2-4 - Invasive mechanical ventilation											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	1/44 (2.3%)	2/35 (5.7%)	**RR 0.40** (0.04 to 4.21)	**34 fewer per 1,000** (from 55 fewer to 183 more)	⨁◯◯◯ Very low
Antigen reactivity score 5-7 vs. score 2-4 - Mortality											
1	non-randomised studies	serious[a]	serious[b]	not serious	serious[c]	none	0/44 (0.0%)	1/35 (2.9%)	**RR 0.27** (0.01 to 6.35)	**21 fewer per 1,000** (from 28 fewer to 153 more)	⨁◯◯◯ Very low

CI=confidence interval; ITU=intensive therapy unit; PUAT=pneumococcal urinary antigen test; RR=risk ratio
a. Single study at serious risk of bias
b. Downgraded once for single study.
c. Downgraded once for crossing one clinical decision threshold (1.25)
d. Downgraded twice for crossing both clinical decision thresholds (0.8 and 1.25)

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

Table 14 Economic evidence table, Xie 2017

Study	Study type	Study quality	Setting	Intervention	Comparator	Participant characteristics	Methods of analysis	Results[a]	Limitations	Additional comments
Xie 2017	Cost effectiveness study Decision analytical model	Partly applicable[b]	Canada Tertiary care hospital	Urine antigen test (BinaxNOW-SP testing for streptococcus pneumoniae) and culture. Both taken at the same time with results of the urine antigen test in an hour and the results of the cultures in 48 hours.	Culture alone. The results of the culture available in 48 hours.	Adult patients admitted to hospital with community acquired pneumonia.	Sensitivity and specificity of both urine antigen test and cultures was taken from a latent-class meta-analysis. Expert opinion was used for inputs such as prevalence as the meta-analysis did not provide a useful estimate. Time horizon was 3 days. Perspective was from a single tertiary hospital. Outcome: Percentage of patients correctly classified. Costs included were cost of antibiotics and tests, nursing time was excluded.	Percentage of patients correctly classified: Urine antigen test and culture: 91.8 Culture alone: 85.6 Costs per patient: Urine antigen test and culture: £53.85 Culture alone: £26.08 Incremental (urine antigen test and culture vs culture alone): Percentage of patients correctly identified: 6.2 Cost: £27.77 Incremental (urine antigen test and culture vs culture alone) cost per case correctly classified: £449.05 Deterministic sensitivity analysis: The cost of the urine antigen test was the main driver of the model. The prevalence of streptococcus pneumoniae and the cost of antibiotics had little effect on the cost effectiveness.	Expert assumptions used for baseline outcomes. Single hospital perspective rather than national. Limitations identified by authors: Difficult to evaluate a new diagnostic test in the absence of a gold standard. QALYs not used as it was not felt to be useful in a diagnostic test assessment.	Source of funding: Not reported Authors' conclusions: "The methods we have described allow us to evaluate the accuracy and economic value of a new test in the absence of a perfect reference test using an evidence-based approach".

Abbreviations: QALY: Quality-Adjusted Life-Years

(a) All costs converted from CAD to GBP using EPPI-Centre Cost Converter
(b) Canadian study based on a single tertiary care hospital in Montreal, cost effectiveness study rather than a cost utility study

Table 15 Economic evidence table, CG191

Study	Study type	Study quality	Setting	Intervention	Comparator	Participant characteristics	Methods of analysis	Results	Limitations	Additional comments
CG191	Cost utility study Decision tree	Directly applicable[(a)]	UK Hospital	[1] No testing (clinical judgement) [2] Blood culture [3] Sputum culture [4] Urinary pneumococcal antigen [5] Urinary legionella antigen [6] Combination of a blood culture and a sputum culture [7] Combination of a blood culture, a urinary pneumococcal antigen and a urinary legionella antigen [8] All tests in combination	All interventions were compared to each other.	Adult patients admitted to hospital with community acquired pneumonia.	Patient characteristics were obtained from hospital episode statistics. The prevalence of pathogens was based on BTS guidelines. Test costs were estimated using expert opinion and hospital treatment costs came from NHS reference costs. Antibiotic costs were obtained from MIMS online. Sensitivity and specificity data were derived from systematics reviews and expert opinions. Mortality data was taken from Lim et al 2001 and supplemented with expert opinions.	Lifetime costs per patient: [1] £2,570 [2] £2,582 [3] £2,664 [4] £2,589 [5] £2,610 [6] £2,683 [7] £2,642 [8] £2,731 Lifetime QALYs per patient: [1] 7.349 [2] 7.367 [3 7.407 [4] 7.349 [5] 7.349 [6] 7.410 [7] 7.367 [8] 7.410 Net monetary benefit (NMB): [1] £144,406 [2] £144,758 [3] £145,468 [4] £144,387 [5] £144,366 [6] £145,524	Key model inputs, including diagnostic accuracy and effectiveness, based on expert opinion due to a lack of evidence. Quality of life data based on sepsis population due to a lack of data in the pneumonia population.	Source of funding: NICE Guideline Authors' conclusions: In the base case blood culture and sputum culture were the most cost-effective options.

Study	Study type	Study quality	Setting	Intervention	Comparator	Participant characteristics	Methods of analysis	Results	Limitations	Additional comments
							Time horizon: Lifetime Perspective: NHS and PSS Outcome: QALYs (based on EQ-5D-3L) Costs included were cost of tests, cost of days in hospital, cost of antibiotics.	[7] £144,698 [8] £145,475 Blood culture [2] and sputum culture [3] was the preferred option. Deterministic sensitivity analysis: Multiple inputs were assessed in sensitivity analyses including changing mortality assumptions, removing sputum culture from the model, changing the prevalence of pathogens, changing the quality-of-life assumptions, reducing the test sensitivities. Several sensitivity analyses on mortality assumptions, prevalence of pathogens, and quality-of-life assumptions showed that the combination of all tests [8] was the most cost-effective strategy. However, in the majority of the sensitivity analyses, the combination of a blood culture [2] and a sputum culture [3] remained the preferred strategy.		

Abbreviations: BTS: British Thoracic Society; EQ-5D-3L: EuroQol Five Dimensions and Three Levels Questionnaire; MIMS: Monthly Index of Medical Specialities; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; NMB: Net Monetary Benefit; PSS: Personal Social Services; QALY: Quality-Adjusted Life-Years; UK: United Kingdom.

(a) UK study, QALYs as an outcome measure

(b) Multiple inputs were based on committee assumptions including the sensitivity and specificity of tests, mortality assumptions

Appendix I – Health economic model

No original health economic modelling was completed for this review question

Appendix J – Excluded studies

Clinical

Study	Reason
Abu Elkhashab, A.E., Swelem, R.S., Abd Alla, A.E.D.A. et al. (2014) Etiological and prognostic values of procalcitonin in hospital-acquired pneumonia. Egyptian Journal of Chest Diseases and Tuberculosis 63(1): 201-206	- Study does not report any of the results specified in the protocol
Agarwal, Mehul, Joshi, Madhur, Gupta, Manohar et al. (2021) Role of blood urea nitrogen and serum albumin ratio in predicting severity of community acquired pneumonia (CAP). Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace 92(3)	- Study does not report any of the results specified in the protocol
Anonymous (1987) Community-acquired pneumonia in adults in British hospitals in 1982-1983: a survey of aetiology, mortality, prognostic factors and outcome. The British Thoracic Society and the Public Health Laboratory Service. The Quarterly journal of medicine 62(239): 195-220	- Not a relevant study design *Exclude on date*
As, A.K., Pala, A.A., Guvenc, O. et al. (2022) Can the blood urea nitrogen to serum albumin ratio be used as a mortality predictor in patients with pneumonia after cardiac surgery?. European Research Journal 8(2): 155-161	- No microbiological test
Benenson, Ronald S, Kepner, Andrew M, Pyle, Donald N 2nd et al. (2007) Selective use of blood cultures in emergency department pneumonia patients. The Journal of emergency medicine 33(1): 1-8	- Already included in previous version of the review. No new data.
Cao, Lin-Feng, Cheng, Jia-Yi, Xu, Zheng et al. (2022) Serum 8-Hydroxydeoxyguanosine Is a Potential Indicator for the Severity and Prognosis in Patients with Community-Acquired Pneumonia: A Prospective Cohort Study. Journal of immunology (Baltimore, Md. : 1950) 208(2): 321-327	- Study does not report any of the results specified in the protocol *No intervention of interest*
Covino, Marcello, Piccioni, Andrea, Bonadia, Nicola et al. (2020) Early procalcitonin determination in the emergency department and clinical outcome of community-acquired pneumonia	- Study does not report any of the results specified in the protocol

Study	Reason
in old and oldest old patients. European journal of internal medicine 79: 51-57	
Dedier, J., Singer, D.E., Chang, Y. et al. (2001) Processes of care, illness severity, and outcomes in the management of community-acquired pneumonia at academic hospitals. Archives of Internal Medicine 161(17): 2099-2104	- Already included in previous version of the review. No new data.
Fine, M J, Orloff, J J, Arisumi, D et al. (1990) Prognosis of patients hospitalized with community-acquired pneumonia. The American journal of medicine 88(5n): 1n-8n	- Not a relevant study design *Exclude on date*
Flyman, S.; Hermansson, A.; Gisselsson-Solen, M. (2020) Nasopharyngeal cultures in children; when, what and why?. International Journal of Pediatric Otorhinolaryngology 130: 109832	- Does not contain a population of people with pneumonia
Garbino, J, Sommer, R, Gerber, A et al. (2002) Prospective epidemiologic survey of patients with community-acquired pneumonia requiring hospitalization in Switzerland. International journal of infectious diseases 6(4): 288-293	- Not a relevant study design *Exclude on date*
Guillotin, Florian, Poulain, Cecile, Gaborit, Benjamin et al. (2022) Potential Impact of Rapid Multiplex PCR on Antimicrobial Therapy Guidance for Ventilated Hospital-Acquired Pneumonia in Critically Ill Patients, A Prospective Observational Clinical and Economic Study. Frontiers in cellular and infection microbiology 12: 804611	- Study does not report any of the results specified in the protocol *Ventilator associated pneumonia not included*
Guo, Shuren; Mao, Xiaohuan; Liang, Ming (2018) The moderate predictive value of serial serum CRP and PCT levels for the prognosis of hospitalized community-acquired pneumonia. Respiratory research 19(1): 193	- Study does not report any of the results specified in the protocol
Haessler, Sarah, Lindenauer, Peter K, Zilberberg, Marya D et al. (2020) Blood Cultures Versus Respiratory Cultures: 2 Different Views of Pneumonia. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 71(7): 1604-1612	- Study does not report any of the results specified in the protocol
Hickey, R W; Bowman, M J; Smith, G A (1996) Utility of blood cultures in pediatric patients found to have pneumonia in the	- Study does not report any of the results specified in the protocol

Study	Reason
emergency department. Annals of emergency medicine 27(6): 721-5	
Ikegame, Satoshi, Wakamatsu, Kentaro, Kumazoe, Hiroyuki et al. (2012) A retrospective analysis of 111 cases of pneumococcal pneumonia: clinical features and prognostic factors. Internal medicine (Tokyo, Japan) 51(1): 37-43	- No microbiological test
Ito, Yutaka, Iwashima, Satoru, Hayano, Satoshi et al. (2018) Rapid Detection of the Macrolide Sensitivity of Pneumonia-Causing Mycoplasma pneumoniae Using Quenching Probe Polymerase Chain Reaction (GENECUBE R). Molecular diagnosis & therapy 22(6): 737-747	- Study does not report any of the results specified in the protocol
Karsas, M.; Becker, P.J.; Green, R.J. (2016) Serious bacterial infections in febrile young children: Lack of value of biomarkers. SAJCH South African Journal of Child Health 10(1): 33-36	- Does not contain a population of people with pneumonia
Kaya, Y., Tas, N., Canakci, E. et al. (2018) Relationship of neutrophil-to-lymphocyte ratio with presence and severity of pneumonia. Journal of Clinical and Analytical Medicine 9(5): 452-457	- No microbiological test
Kim, J.E., Kim, U.J., Kim, H.K. et al. (2014) Predictors of viral pneumonia in patients with community-acquired pneumonia. PLoS ONE 9(12): e114710	- Study does not report any of the results specified in the protocol
Liu, W.W. and Liang, Y.F. (2018) Increased expression of TIM-1 predicts the progression of pneumonia in pediatric patients. International Journal of Clinical and Experimental Medicine 11(5): 4875-4882	- Study does not report any of the results specified in the protocol *post-operative pneumonia and these tests are all biomarker tests rather than microbiological*
Lui, Grace, To, Heather K W, Lee, Nelson et al. (2020) Adherence to Treatment Guideline Improves Patient Outcomes in a Prospective Cohort of Adults Hospitalized for Community-Acquired Pneumonia. Open forum infectious diseases 7(5): ofaa146	- No microbiological test
Lupisan, S.P., Ruutu, P., Erma Abucejo-Ladesma, P. et al. (2007) Predictors of death from severe pneumonia among children 2-59 months old hospitalized in Bohol, Philippines: Implications for referral criteria at a first-level health facility. Tropical	- Does not contain a population of people with pneumonia

Study	Reason
Medicine and International Health 12(8): 962-971	
Matsui, K., Kawakubo, H., Matsuda, S. et al. (2021) Clinical usefulness of sputum culture on the first postoperative day to predict early postoperative pneumonia after esophagectomy for esophageal cancer. Esophagus 18(4): 773-782	- Study does not report any of the results specified in the protocol
McCulloh, Russell J, Koster, Michael P, Yin, Dwight E et al. (2015) Evaluating the use of blood cultures in the management of children hospitalized for community-acquired pneumonia. PloS one 10(2): e0117462	- Study does not report any of the results specified in the protocol
Pickens, Chiagozie I, Qi, Chao, Postelnick, Michael et al. (2021) Association between a rapid diagnostic test to detect methicillin-resistant Staphylococcus Aureus pneumonia and decreased vancomycin use in a medical intensive care unit over a 30-month period. Infection control and hospital epidemiology 42(11): 1385-1387	- Study does not report any of the results specified in the protocol
Poole, Stephen, Tanner, Alex R, Naidu, Vasanth V et al. (2022) Molecular point-of-care testing for lower respiratory tract pathogens improves safe antibiotic de-escalation in patients with pneumonia in the ICU: Results of a randomised controlled trial. The Journal of infection 85(6): 625-633	- No microbiological test
Ramgopal, Sriram, Cotter, Jillian M, Navanandan, Nidhya et al. (2023) Viral Detection Is Associated With Severe Disease in Children With Suspected Community-Acquired Pneumonia. Pediatric emergency care 39(7): 465-469	- Study does not report any of the results specified in the protocol
Schulert, Grant S; Hain, Paul D; Williams, Derek J (2014) Utilization of viral molecular diagnostics among children hospitalized with community acquired pneumonia. Hospital pediatrics 4(6): 372-6	- Study does not report any of the results specified in the protocol
Sellares-Nadal, Julia, Burgos, Joaquin, Velasquez, Fernando et al. (2023) Impact of viral detection in patients with community-acquired pneumonia: An observational cohort study. Medicina clinica 161(12): 523-529	- Study does not report any of the results specified in the protocol

Study	Reason
Serrano, Leyre, Ruiz, Luis Alberto, Perez-Fernandez, Silvia et al. (2023) Short- and long-term prognosis of patients with community-acquired Legionella or pneumococcal pneumonia diagnosed by urinary antigen testing. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases 134: 106-113	- No microbiological test
Skovgaard, Marlene, Schonheyder, Henrik C, Benfield, Thomas et al. (2013) Impact of positive chest X-ray findings and blood cultures on adverse outcomes following hospitalized pneumococcal lower respiratory tract infection: a population-based cohort study. BMC infectious diseases 13: 197	- No microbiological test
Teng, Fei, Liu, Xin, Guo, Shu-Bin et al. (2019) Community-acquired bacterial co-infection predicts severity and mortality in influenza-associated pneumonia admitted patients. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy 25(2): 129-136	- Study does not report any of the results specified in the protocol
Ugajin, Motoi, Yamaki, Kenichi, Hirasawa, Natsuko et al. (2014) Predictive values of semi-quantitative procalcitonin test and common biomarkers for the clinical outcomes of community-acquired pneumonia. Respiratory care 59(4): 564-73	- Study does not report any of the results specified in the protocol *Exclude - biomarkers*
van der Eerden, M.M., Vlaspolder, F., de Graaff, C.S. *et al.* (2005) Value of intensive diagnostic microbiological investigation in low- and high-risk patients with community-acquired pneumonia. *Eur J Clin Microbiol Infect Dis* 24, 241–249.	- Already included in previous version of the review. No new data.
Wei, Jianhua, Zang, Na, Zhang, Jing et al. (2023) Genome and proteomic analysis of risk factors for fatal outcome in children with severe community-acquired pneumonia caused by human adenovirus 7. Journal of medical virology 95(11): e29182	- Study does not report any of the results specified in the protocol *PICU patients on MV*
Yang, Tianjun, Mei, Qing, Fang, Xiaowei et al. (2022) Clinical Value of Metagenomics Next-Generation Sequencing in Bronchoalveolar Lavage Fluid for Patients with Severe Hospital-Acquired Pneumonia: A Nested Case-Control Study. Infection and drug resistance 15: 1505-1514	- Study does not report any of the results specified in the protocol *BL excluded*

Study	Reason
Zhang, Yin, Lin, Jilei, Shi, Qingxia et al. (2020) Diagnostic accuracy of time to first positivity of blood cultures for predicting severe clinical outcomes in children with pneumonia-related bacteremia. Journal of investigative medicine : the official publication of the American Federation for Clinical Research 68(7): 1241-1249	- Study does not report any of the results specified in the protocol

BL= bronchoalveolar lavage ; MV= mechanical ventilation; PICU=paediatric intensive care unit

Economic

Study	Code [Reason]
Akyil, Fatma Tokgoz, Hazar, Armagan, Erdem, Ipek et al. (2015) Hospital Treatment Costs and Factors Affecting These Costs in Community-Acquired Pneumonia. Turkish thoracic journal 16(3): 107-113	- Study does not contain a relevant intervention *Costing study, does not compare interventions*
Andrews, Annie Lintzenich, Simpson, Annie N, Heine, Daniel et al. (2015) A Cost-Effectiveness Analysis of Obtaining Blood Cultures in Children Hospitalized for Community-Acquired Pneumonia. The Journal of pediatrics 167(6): 1280-6	- US study
Antunes, C, Pereira, M, Rodrigues, L et al. (2020) Hospitalization direct cost of adults with community-acquired pneumonia in Portugal from 2000 to 2009. Pulmonology 26(5): 264-267	- Study does not contain a relevant intervention *Costing study, does not compare interventions*
Asti, L, Bartsch, S M, Umscheid, C A et al. (2019) The potential economic value of sputum culture use in patients with community-acquired pneumonia and healthcare-associated pneumonia. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 25(8): 1038e1-1038e9	- US study
Buendia, Jefferson A and Patino, Diana Guerrero (2023) Corticosteroids for the treatment of respiratory infection by Mycoplasma pneumoniae in children: A cost-utility analysis. Pediatric pulmonology 58(10): 2809-2814	- Non OECD country *Columbia*

Study	Code [Reason]
Cammarota, Gianmaria; Vetrugno, Luigi; Longhini, Federico (2023) Lung ultrasound monitoring: impact on economics and outcomes. Current opinion in anaesthesiology 36(2): 234-239	- Does not contain a population of people with only pneumonia, includes people with acute respiratory failure *Unclear if the patients are intubated* - US study *Unclear if the study is US or Europe* -Abstract only
Ceyhan, Mehmet, Ozsurekci, Yasemin, Aykac, Kubra et al. (2018) Economic burden of pneumococcal infections in children under 5 years of age. Human vaccines & immunotherapeutics 14(1): 106-110	- Study does not contain a relevant intervention *Non-comparative costing analysis*
Cisco, Giulio, Meier, Armando N, Senn, Nicolas et al. (2024) Cost-effectiveness analysis of procalcitonin and lung ultrasonography guided antibiotic prescriptions in primary care. The European journal of health economics : HEPAC : health economics in prevention and care	- setting in primary care whereas the review was in secondary care
Costa, Nadege, Hoogendijk, Emiel O, Mounie, Michael et al. (2017) Additional Cost Because of Pneumonia in Nursing Home Residents: Results From the Incidence of Pneumonia and Related Consequences in Nursing Home Resident Study. Journal of the American Medical Directors Association 18(5): 453e7-453e12	- Study does not contain a relevant intervention *Non-comparative costing analysis*
Hyams, Catherine; Williams, O Martin; Williams, Philip (2020) Urinary antigen testing for pneumococcal pneumonia: is there evidence to make its use uncommon in clinical practice?. ERJ open research 6(1)	- Review article but not a systematic review, all primary studies were checked for relevance
Ito, Akihiro, Ishida, Tadashi, Tokumasu, Hironobu et al. (2017) Impact of procalcitonin-guided therapy for hospitalized community-acquired pneumonia on reducing antibiotic consumption and costs in Japan. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy 23(3): 142-147	- Not a relevant study design *Costing study not a cost utility/ effectiveness study*
Javanbakht, Mehdi, Moradi-Lakeh, Maziar, Mashayekhi, Atefeh et al. (2022) Continuous Monitoring of Respiratory Rate with Wearable Sensor in Patients Admitted to Hospital with Pneumonia Compared with Intermittent Nurse-Led Monitoring in the	- Study does not contain a relevant intervention *Continuous monitoring versus intermittent monitoring, NEWS used in both arms*

Study	Code [Reason]
United Kingdom: A Cost-Utility Analysis. PharmacoEconomics - open 6(1): 73-83	
Khole, Aalok V, Dionne, Emily, Zitek-Morrison, Emily et al. (2023) Cefepime extended infusion versus intermittent infusion: Clinical and cost evaluation. Antimicrobial stewardship & healthcare epidemiology : ASHE 3(1): e119	- US study
Latif, Marina, Guo, Ning, Tereshchenko, Larisa G et al. (2023) Association of hospital spending with care patterns and mortality in patients hospitalized with community-acquired pneumonia. Journal of hospital medicine 18(11): 986-993	- Study does not contain a relevant intervention *US costing study with no comparative interventions*
Leem, Ah Young, Jung, Won Jai, Kang, Young Ae et al. (2014) Comparison of methicillin-resistant Staphylococcus aureus community-acquired and healthcare-associated pneumonia. Yonsei medical journal 55(4): 967-74	- Not a relevant study design *Not a health economic study*
Macaya, M.C.; Ridulfo, A.H.; Ramirez-Santana, M. (2015) Comparison of costs and health outcomes of users with community-acquired pneumonia treated at home or in traditional hospitalization: An exploratory study of 40 cases. Value in Health Regional Issues 8: 112-115	- Study not reported in English *Reported in Spanish*
McKinnell, James A, Corman, Shelby, Patel, Dipen et al. (2018) Effective Antimicrobial Stewardship Strategies for Cost-effective Utilization of Telavancin for the Treatment of Patients With Hospital-acquired Bacterial Pneumonia Caused by Staphylococcus aureus. Clinical therapeutics 40(3): 406-414e2	- Study does not contain a relevant intervention *US study that compares different antibiotics rather than length of treatments*
Meacock, Rachel, Sutton, Matt, Kristensen, Soren Rud et al. (2017) Using Survival Analysis to Improve Estimates of Life Year Gains in Policy Evaluations. Medical decision making : an international journal of the Society for Medical Decision Making 37(4): 415-426	- Study does not contain a relevant intervention *Modelling survival not cost effectiveness of treatment*
Miners, Lisa, Huntington, Susie, Lee, Nathaniel et al. (2023) An economic evaluation of two PCR-based respiratory panel assays for patients admitted to hospital with community-acquired	- Not a relevant study design *Cost consequence study*

Study	Code [Reason]
pneumonia (CAP) in the UK, France and Spain. BMC pulmonary medicine 23(1): 220	
Patel, Archana B, Bang, Akash, Singh, Meenu et al. (2015) A randomized controlled trial of hospital versus home based therapy with oral amoxicillin for severe pneumonia in children aged 3 - 59 months: The IndiaCLEN Severe Pneumonia Oral Therapy (ISPOT) Study. BMC pediatrics 15: 186	- Non OECD country *India*
Pliakos, Elina Eleftheria, Andreatos, Nikolaos, Tansarli, Giannoula S et al. (2019) The Cost-Effectiveness of Corticosteroids for the Treatment of Community-Acquired Pneumonia. Chest 155(4): 787-794	- US study
Prasath, T.M., Ramachandran, V., Geetha, S. et al. (2019) Hidden Markov model-based cough sound analysis for classification of asthma and pneumonia in pediatric. Drug Invention Today 11(7): 1692-1695	- Full text paper not available
Przybilla, Jens, Ahnert, Peter, Bogatsch, Holger et al. (2020) Markov State Modelling of Disease Courses and Mortality Risks of Patients with Community-Acquired Pneumonia. Journal of clinical medicine 9(2)	- Study does not contain a relevant intervention *Does not include costs*
Reynolds, Courtney A, Finkelstein, Jonathan A, Ray, G Thomas et al. (2014) Attributable healthcare utilization and cost of pneumonia due to drug-resistant streptococcus pneumonia: a cost analysis. Antimicrobial resistance and infection control 3: 16	- Study does not contain a relevant intervention *Looking at different antibiotics not the length of the courses*
Rozenbaum, Mark H, Mangen, Marie-Josee J, Huijts, Susanne M et al. (2015) Incidence, direct costs and duration of hospitalization of patients hospitalized with community acquired pneumonia: A nationwide retrospective claims database analysis. Vaccine 33(28): 3193-9	- Study does not contain a relevant intervention *Costing analysis without comparators*
Shi, Honghao, Guo, Wanjie, Zhu, He et al. (2019) Cost-Effectiveness Analysis of Xiyanping Injection (Andrographolide Sulfonate) for Treatment of Adult Community Acquired Pneumonia: A Retrospective, Propensity Score-Matched	- Study does not contain a relevant intervention *Andrographolide Sulfonate injection*

Study	Code [Reason]
Cohort Study. Evidence-based complementary and alternative medicine : eCAM 2019: 4510591	
Shiri, Tinevimbo, Khan, Kamran, Keaney, Katherine et al. (2019) Pneumococcal Disease: A Systematic Review of Health Utilities, Resource Use, Costs, and Economic Evaluations of Interventions. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research 22(11): 1329-1344	- Study does not contain a relevant intervention *Vaccines and antibiotics (not length of treatment)*
Sultana, Marufa, Sarker, Abdur Razzaque, Ali, Nausad et al. (2019) Economic evaluation of community acquired pneumonia management strategies: A systematic review of literature. PloS one 14(10): e0224170	- Study does not contain a relevant intervention *Different antibiotics in adults and bubble continuous positive airway pressure in newborns*
Tesfaye, Solomon H, Loha, Eskindir, Johansson, Kjell Arne et al. (2022) Cost-effectiveness of pulse oximetry and integrated management of childhood illness for diagnosing severe pneumonia. PLOS global public health 2(7): e0000757	- Non OECD country *Ethiopia*
Torres, Antoni, Bassetti, Matteo, Welte, Tobias et al. (2020) Economic analysis of ceftaroline fosamil for treating community-acquired pneumonia in Spain. Journal of medical economics 23(2): 148-155	- Study does not contain a relevant intervention *Different antibiotics not different durations*
Wagner, A P, Enne, V I, Livermore, D M et al. (2020) Review of health economic models exploring and evaluating treatment and management of hospital-acquired pneumonia and ventilator-associated pneumonia. The Journal of hospital infection 106(4): 745-756	- Study does not contain a relevant intervention *Different antibiotics not different durations*
Zhang, Shanshan, Sammon, Peter M, King, Isobel et al. (2016) Cost of management of severe pneumonia in young children: systematic analysis. Journal of global health 6(1): 010408	- Study does not contain a relevant intervention *Costing study with no outcomes*

OECD=the organisation for economic co-operation and development

Appendix K– Research recommendations – full details

K1.1 Research recommendation

Which microbiological test, or group of tests, can aid decision making around safely reducing inappropriate antibiotic prescribing in people with suspected pneumonia, community or hospital-acquired?

K1.1.1 Why this is important

Microbiological tests, including blood and sputum cultures, may inform decisions to reduce rates of empirical prescribing and support more directed antibiotic therapy but the evidence on this remains limited. Point of care tests and multiple pathogen panels could help to direct the treatment approach within less than 24 hours. These tests could also help to safely identify patients who do not require antibiotics. The burden of community acquired pneumonia is large, and its treatment accounts for a high proportion of antibiotic use in hospitals. Overuse of antibiotics is associated with antimicrobial resistance, which is a national and global priority.

K1.1.2 Rationale for research recommendation

Importance to 'patients' or the population	Microbiological tests could help to ensure patients receive the right antibiotic treatment, or are not given antibiotics when they do not require them. For individual patients, this would help to support quicker and more effective treatment, and for the population, this would prevent the overuse of antibiotics and support antimicrobial stewardship.
Relevance to NICE guidance	The guideline recommends different types of microbiological testing depending on the pneumonia severity and several other factors. This research would help to further clarify which tests are most effective for which groups.
Relevance to the NHS	This would help with antimicrobial stewardship, which is a national and global priority.
National priorities	High – antimicrobial stewardship is a national priority.
Current evidence base	No UK based data and limited RCT evidence.
Equality considerations	No direct considerations

NICE=national institute for health and care excellence; RCT=randomised controlled trial;

K1.1.3 Modified PICO table

Population	People diagnosed with pneumonia (CAP or HAP)
Intervention	Microbiological tests, alone or in combination, including blood and sputum cultures. Point of

	care tests and multiple pathogen panels should be included. For RCTs, treatment based on test results.
Comparator	Standard care (including standard microbiological tests, where appropriate) For RCTs, treatment based on test results.
Outcome	• Antibiotic use – duration, type, route of administration • Change in antibiotic and choice of antibiotic (broad or narrow spectrum) • Antibiotic side effects • Adverse events, including *C.diff* • Hospital admission and readmission • ICU admission • Cost-effectiveness
Study design	Test and treat RCTs
Timeframe	1 month
Additional information	None

ICU=intensive care unit; RCT=randomised controlled trial