National Institute for Health and Care Excellence

Pneumonia: diagnosis and management

[J] Evidence review for pneumonia outcome prediction tools for babies, children and young people presenting to primary care

NICE guideline NG250
Evidence review underpinning a research recommendation in the NICE guideline

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Final

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1.1 Review question

In babies, children and young people with suspected community-acquired pneumonia who present to primary care, what is the most accurate and cost-effective outcome prediction tool to identify under 18s whose outcome would be likely to benefit by referral to hospital?

1.1.1 Introduction

Most children presenting to primary care with symptoms such as cough and fever have a mild, often viral infection with a favourable natural course. However, physicians must always be cautious of potentially serious infections such as pneumonia which may require hospital admission. The distinction between mild and more serious illness can be difficult, particularly at first presentation in primary care in the early stages of the illness. GPs often have to decide whether to rule out more serious infection and treat the child at home, or when immediate medical treatment or referral to secondary care is needed. This is primarily done using clinical history taking and examination, but clinical prediction models or outcome prediction tools may support this decision making. This review aimed to evaluate the prognostic accuracy of prediction tools for determining which children with suspected community-acquired pneumonia would benefit from referral for hospital care.

1.1.2 Summary of the protocol

Table 1: Summary inclusion criteria

Population	**Inclusion** Babies over 28 days (corrected gestational age), children and young people (age <18 years) with suspected community-acquired pneumonia presenting to primary care. Where insufficient evidence is found from studies including pneumonia patients only (or where >75% of the study population have pneumonia), evidence from studies including children with suspected lower respiratory tract infection (LRTI) will be included but will be downgraded once for indirectness. **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.
Prognostic tool	Any risk assessment tool that uses a collection of respiratory and fever-based symptoms or a prediction model based on a collection of symptoms. Individual symptoms predictive of hospital admission will not be included unless part of a risk prediction model.
Comparator	N/A
Outcomes	• Admission to hospital • Admission to ICU • Admission to acute respiratory unit • Length of stay (in any of the above settings) • Primary care re-attendance with CAP (as a marker of failure of original decision)
Measures	<u>Discrimination measures:</u> • Concordance (C) statistic, area under the curve (AUC) with 95% confidence interval <u>Calibration measures:</u> • number of observed (O) and expected (E) events • total O:E ratio • calibration slope Where available, the following measures will be reported: • adjusted hazard ratios (HR), adjusted odds ratios (OR) or adjusted risk ratios (RR).
Study type	**Inclusion** • Prospective or retrospective observational cohorts or cross-sectional studies which evaluate the performance of the risk prediction tools. These studies should include a multivariate analysis which accounts for key confounders. Key confounders will vary based on each risk factor but should at least include age and sex. • Validation studies • Systematic reviews of the above study types

	Exclusion • Case-control studies, derivation and internal validation studies

For the full protocol see appendix A.

1.1.3 Methods and process

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

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

Protocol deviations

The protocol specified that studies evaluating the performance of risk prediction tools should include a multivariate analysis which accounts for key confounders, and that key confounders would vary based on each risk factor but should at least include age and sex. When reviewing possible includes at full text, it was noted that only 1 of the possible includes reported analyses that adjusted for confounding variables (Gallagher 2021). In order to make most use of the limited evidence available in this area, a protocol deviation was agreed so that otherwise eligible studies that did not adjust for confounding could be included in the evidence review.

The protocol listed prognostic outcomes including c-statistic and area under the curve. In order to make the most use of the available data, additional outcomes not originally listed in the protocol were extracted: sensitivity, specificity, positive likelihood ratio and negative likelihood ratio.

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 prognostic evidence were run on 24 September 2024. The search aimed to cover the named tools STARWAVe and Feverkidstool, as well as identifying other appropriate prediction tools that had not been named in the protocol. 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. Standard NICE filters were used to limit to cohort, cross-sectional and validation studies.

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 19 September 2024 using seed references identified from the scoping searches 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 validated NICE Cost Utility Filter was used on MEDLINE and Embase. Validated NICE filters were used in MEDLINE and Embase to remove references exclusively set in countries that are not OECD members.

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 Prognostic evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 3,948 references (see appendix B for the literature search strategy). These 3,948 references were screened at title and abstract level against the review protocol, with 3,911 excluded at this level. The full texts of 37 studies were ordered for closer inspection. 4 of these studies met the criteria specified in the review protocol (appendix A). All 4 studies were prospective cohort studies that externally validated clinical prediction models. There were 4 different models validated: the Feverkidstool, the Craig model, the 'Difficulty drawing breath' model, and the STARWAVe tool. Two studies (Gallagher 2021 and Wildes 2021) used the same study population to validate 2 different models (the 'Difficulty drawing breath' model and the STARWAVe tool). For a summary of the 4 included studies see table 2, and for a summary of the models, see section 1.1.5.1.

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 prognostic evidence

Table 2: Summary of studies included in the prognostic evidence

Study details	Setting and Location	Population	Prognostic model(s)	Outcome predicted	Rate of hospitalisation	Outcomes reported	Risk of bias and study applicability
Bos 2023 Prospective cohort study External validation of 4 clinical prediction models[a]	Setting: 92 general practices, 6 outpatient paediatric practices and 6 emergency departments Location: Belgium	Children aged 1 month to 16 years presenting to primary care with an acute illness N = 8211	1. Feverkidstool 2. Craig model	Serious infection requiring hospital admission for more than 24 hours (results reported for pneumonia subgroup; 171/8211)	498/8211 (6.07%)	• C-statistic • Calibration intercept and calibration slope • Sensitivity and specificity • +LR and -LR	Low risk of bias Partially indirect
Gallagher 2021 Prospective cohort study	Setting: 2 primary care facilities – a community health centre (n=484) and the outpatient department of a central hospital (n=10). Location: Malawi	Children aged 2-59 months with CAP N = 494	'Difficulty drawing breath' model	Hospitalisation (within 30 days)	56/488 (11.5%)	• Area under the curve (AUC) • Sensitivity and specificity	Moderate risk of bias Partially indirect
Hay 2016 Prospective cohort study	Setting: 247 primary care practices Location: UK	Children aged 3 months - 16 years presenting to primary care with acute cough and other	STARWAVe clinical prediction rule	Hospitalisation (within 30 days)	78/8394 (0.9%) [only 15 were admitted on day 1, the rest was during the 30 day follow-up period)	• Area under the curve (AUC) • Sensitivity and specificity	Low risk of bias Partially indirect

Study details	Setting and Location	Population	Prognostic model(s)	Outcome predicted	Rate of hospitalisation	Outcomes reported	Risk of bias and study applicability
		respiratory tract infection (RTI) symptoms N = 8394				• Risk of hospital admission	
Wildes 2021 External validation of STARWAVe tool	Setting: 2 primary care facilities – a community health centre (n=484) and the outpatient department of a central hospital (n=10). Location: Malawi	Children aged 2-59 months with CAP N = 494	STARWAVe clinical prediction rule	Hospitalisation (within 30 days)	56/494 (11.3%) 19% of admissions were on the same day as attending primary care	• Area under the curve (AUC) • Sensitivity and specificity • Risk of hospital admission	Moderate risk of bias Indirect

Notes
CAP: Community acquired pneumonia
[a] Bos 2023 reports on the external validation of 4 models, but the serious bacterial infections (SBI) model is not included in this review because separate data for pneumonia is not reported; results are for all serious bacterial infections, and the Paediatric Advanced Warning Score (PAWS) is not included because this model was developed to predict the risk of serious illness, which is broader than serious infections, and does not report separate data for pneumonia.

See appendix D for full evidence tables.

1.1.5.1 Prognostic model summaries

1.1.5.1.1 Feverkidstool (developed by Nijman 2013; validated in Bos 2023)

This clinical prediction model is designed to assess the risk of different serious bacterial infections (including pneumonia) in children with fever attending the emergency department. It was developed using a derivation cohort of 2,717 children aged 1 month to 15 years presenting with fever at the ED of children's hospitals in Rotterdam and the Hague, and externally validated using a second cohort of 487 febrile children attending a paediatric assessment unit in the UK. The outcome categories were pneumonia, other serious bacterial infections (SBIs), and no SBIs. Potential predictors were obtained from keynote research on children with fever and included those which were readily available at first assessment and had small interobserver variability. The final model includes 10 variables: age (<1 year or ≥1 year), sex, body temperature, fever duration, tachypnoea and tachycardia defined by APLS (Advanced Paediatric Life Support group) and categorised using age specific thresholds, oxygen saturation <94%, ill-appearance, peripheral capillary refill time ≥3s, chest wall retractions, and CRP. There is a digital calculator to generate scores and these indicate children at low, intermediate and high risk of pneumonia or other SBIs.

1.1.5.1.2 Craig model (developed by Craig 2010; validated in Bos 2023)

This clinical prediction model predicts the risk of complicated urinary tract infections (cUTI), pneumonia and bacteraemia in feverish children presenting to the emergency department. The model was developed from a cohort of 15,781 children aged <5 years presenting to an Australian ED with a febrile illness. Preliminary analysis of 40 potential signs and symptoms, compiled from a review of the published literature on assessment tools for febrile children and that are routinely elicited in children suspected of having a bacterial infection, were used to select variables for inclusion in a multinomial model. The final model includes 26 items: general appearance, cough, highest temperature (>38ºC), breathing difficulty, abnormal chest sounds, chronic disease, capillary refill time (>2 seconds), urinary symptoms, elevated respiratory rate, chest crackles, pneumococcal vaccine status, elevated heart rate, felt hot, meningococcal vaccine status, infectious contacts, crying, fluid intake, respiratory symptoms, diarrhoea, bulging fontanelle, male, focal bacterial infection, abnormal ear nose and throat signs, age, rash, stridor, and wheeze. The authors suggest that these clinical findings could be entered into a computer program and the risk calculation could be generated to determine the likelihood of pneumonia or other SBIs.

1.1.5.1.3 'Difficulty drawing breath' model (Gallagher 2021)

This model was developed in a study designed to understand the predictors of hospitalisation for pneumonia in children aged 2-59 months in Northern Malawi. In multivariable modelling, 7 variables were predictive of hospitalisation: difficulty breathing, deep breathing, respiratory rate >70 bpm, age <2 years, wheeze, lower chest wall indrawing, and grunting. To create a simplified version of the model, a score of 1 was assigned to each sign or symptom to generate a simple 7-point "Difficulty drawing breath" score. A score of 0–1 is associated with low need for hospitalisation, 2–3 is intermediate and a score of 4 or greater suggests a high need for hospitalisation. For each unit increase in the Difficulty drawing breath score, there is a 10.7% (95%CI: 7.9-13.4%) increase in the likelihood of hospitalisation.

1.1.5.1.4 STARWAVe tool (Hay 2016)

This clinical prediction rule was developed to help identify children presenting to general practice with a respiratory tract infection who are at risk of future hospital admission. It was developed and internally validated using a UK-based cohort of 8394 children aged 3 months to 16 years. Data were collected on a large number of candidate variables: 8 sociodemographic and 4 past medical history items; 33 parent-reported symptoms; and 14 physical examination signs. The final model comprised 7 simple, routinely collected clinical characteristics that were independently associated with hospital admission: age <2 years, current asthma, illness duration of 3 days or less, parent-reported moderate or severe vomiting in the previous 24 hours, parent-reported severe fever in the previous 24 hours or a body temperature of 37.8ºC or more at presentation, clinician-reported intercostal or subcostal recession, and clinician-reported wheeze on auscultation. Assigning a simple 1-point score to each of these characteristics generates an overall STARWAVe score which distinguishes 3 hospital admission risk groups: very low risk (0-1 point), normal risk (2-3 points) and high risk (≥4 points).

1.1.6 Summary of the prognostic evidence

1.1.6.1 C-statistics

Clinical prediction model	Study(s)	No. of participants	C-statistic (95% CI)		Quality
			Original model	Updated model	
Feverkidstool	Bos 2023	8049	0.80 (0.77 to 0.84)	0.83 (0.80 to 0.86)	Low[1,2]
Craig model	Bos 2023	8211	0.80 (0.77 to 0.83)	0.83 (0.80 to 0.86)	Low[1,2]

[1] Downgraded once because study assessed as partially indirect
[2] Downgraded once for inconsistency – single study

1.1.6.2 Area under the curve (AUC)

Clinical prediction model	Study(s)	No. of participants	Area under the curve (95% CI)	Quality
'Difficulty drawing breath' model	Gallagher 2021	494	0.91 (0.87 to 0.95)	Very low[1,2,3]
STARWAVe	Hay 2016	8394	0.81 (0.76 to 0.85)	Very low[2,3,4]
STARWAVe	Wildes 2021	494	0.80 (0.75 to 0.85)	Very low[1,5,3,4]

[1] Downgraded once for moderate concerns about risk of bias
[2] Downgraded once because study assessed as partially indirect
[3] Downgraded once for inconsistency: single study
[4] Downgraded once because 95%CI crosses 1 decision making threshold (test classification accuracy thresholds)
[5] Downgraded twice because study assessed as indirect

1.1.6.3 Calibration statistics

	Study	No. of participants	Effect estimate (95% CI)		Quality
			Original model	Updated model	
Feverkidstool; pneumonia vs absence of SBI					

	Study	No. of participants	Effect estimate (95% CI)		Quality
			Original model	Updated model	
Calibration slope	Bos 2023	8049	1.01 (0.87 to 1.14)	1.04 (0.92 to 1.17)	Low[1,2,3]
Calibration intercept	Bos 2023	8049	0.09 (-0.07 to 0.24)	0.00 (-0.16 to 0.16)	Low[1,2,3]
Craig model; pneumonia vs absence of SBI					
Calibration slope	Bos 2023	8211	0.72 (0.63 to 0.81)	1.05 (0.93 to 1.18)	Low[1,2,3]
Calibration intercept	Bos 2023	8211	-0.87 (-1.03 to -0.71)	0.00 (-0.16 to 0.16)	Low[1,2,3]

[1] Downgraded once because study assessed as partially indirect
[2] Downgraded once for inconsistency: single study
[3] Not possible to assess imprecision

1.1.6.4 Predictive accuracy measures

No. studies	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95% CI)	Quality
Feverkidstool (updated in Bos 2023): Risk ≥2.5% (low risk cut-off). Outcome: pneumonia requiring hospital admission					
1	8049	0.71 (0.64 to 0.78)	0.77 (0.76 to 0.78)	LR+ 3.09 (2.79 to 3.42)	Low[1,2]
				LR- 0.37 (0.29 to 0.47)	Low[1,2]
Feverkidstool (updated in Bos 2023): Risk ≥10% (high risk cut-off). Outcome: pneumonia requiring hospital admission					
1	8049	0.29 (0.22 to 0.36)	0.98 (0.97 to 0.98)	LR+ 12.40 (9.41 to 16.36)	Low[1,2]
				LR- 0.73 (0.66 to 0.80)	Low[1,2]
Feverkidstool (updated in Bos 2023): Risk ≥30% (high risk cut-off). Outcome: pneumonia requiring hospital admission					
1	8049	0.08 (0.04 to 0.13)	1.00 (1.00 to 1.00)	LR+ 31.52 (15.83 to 62.78)	Low[1,2]
				LR- 0.93 (0.89 to 0.97)	Low[1,2]
Craig model (updated in Bos 2023): Risk ≥2.5% (low risk cut-off). Outcome: pneumonia requiring hospital admission					
1	8211	0.69 (0.61 to 0.76)	0.81 (0.80 to 0.81)	LR+ 3.56 (3.19 to 3.97)	Low[1,2]
				LR- 0.38 (0.31 to 0.48)	Low[1,2]

No. studies	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95% CI)	Quality
Craig model (updated in Bos 2023): Risk ≥10% (high risk cut-off). Outcome: pneumonia requiring hospital admission					
1	8211	0.27 (0.21 to 0.35)	0.97 (0.97 to 0.98)	LR+ 10.89 (8.24 to 14.39)	Low[1,2]
				LR- 0.74 (0.68 to 0.82)	Low[1,2]
Craig model (updated in Bos 2023): Risk ≥30% (high risk cut-off). Outcome: pneumonia requiring hospital admission					
1	8211	0.08 (0.04 to 0.13)	1.00 (1.00 to 1.00)	LR+ 43.66 (20.84 to 91.47)	Low[1,2]
				LR- 0.93 (0.89 to 0.97)	Low[1,2]
'Difficulty drawing breath' model (Gallagher 2021): Score ≥3 (intermediate- to high-risk). Outcome: hospitalisation					
1	494	0.88 (0.86 to 0.95)	0.84 (0.80 to 0.87)	LR+ Not reported	-N/A[a]
				LR- Not reported	N/A
STARWAVe (Hay 2016): Normal or high risk vs very low risk. Outcome: hospitalisation within 30 days					
1	8394	0.78 (not reported)	0.68 (not reported)	LR+ Not reported	N/A
				LR- Not reported	N/A
STARWAVe (Hay 2016): High risk vs normal or very low risk. Outcome: hospitalisation within 30 days					
1	8394	0.31 (not reported)	0.98 (not reported)	LR+ Not reported	N/A
				LR- Not reported	N/A
STARWAVe (Wildes 2021): Score ≥4 (high risk)					
1	494	0.32 (0.20 to 0.46)	0.91 (0.88 to 0.94)	LR+ Not reported	N/A
				LR- Not reported	N/A

[1] Downgraded once because study assessed as partially indirect
[2] Downgraded once for inconsistency: single study
[a] GRADE quality assessment applies to LRs (not sensitivity or specificity), so is not provided for outcomes where no LRs are reported.

1.1.6.5 Risk of hospital admission using the STARWAVe rule

STARWAVe risk group	Number of predictors	Hospitalised children	Non-hospitalised children	Risk of hospital admission	
				Risk percentage	95% CI
Hay 2016					
Very low risk	0 to 1	17 (22%)	5576 (68%)	0.3% (1 in 328)	0.2% - 0.4%
Normal risk	2 to 3	37 (47%)	2483 (30%)	1.5% (1 in 68)	1.0% - 1.9%
High risk	4 or more	24 (31%)	180 (2%)	11.8% (1 in 8.5)	7.3% - 16.2%
Total		78 (100%)	8239 (100%)	0.9% (1 in 106)	0.7% - 1.2%
Wildes 2021					
Very low risk	0 to 1	0 (0%)	107 (24.4%)	0%	-
Normal risk	2 to 3	38 (67.9%)	293 (66.9%)	11.5%	8% - 15%
High risk	4 or more	18 (32.1%)	38 (8.7%)	32.1%	20% - 46%
Total		56 (100%)	438 (100%)	11.3%	8% - 14%

See appendix F for full GRADE tables.

1.1.7 Economic evidence

A single search was performed to identify published economic evaluations of relevance to any of the questions in this guideline update. See Appendix B 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. Thirty-three studies were excluded following the full-text review. See Appendix G for the study selection process.

1.1.7.2 Excluded studies

See Appendix J for a list of excluded studies, with reasons for exclusions.

1.1.8 Summary of included economic evidence

No health economic evidence was included

1.1.9 Economic model

No original health economic modelling was done for this review question.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

Area under the curve and c-statistic were used to indicate the usefulness of each test and the committee used established test accuracy thresholds to interpret the values reported, with values of 0.7 to <0.8 representing good classification accuracy, values of 0.8 to <0.9 representing excellent classification accuracy, and values of 0.9 to 1.0 representing outstanding classification accuracy. These outcomes were used in combination with sensitivity, specificity and likelihood ratios to evaluate the performance of each clinical prediction model.

The committee considered the sensitivity and specificity data and discussed the impact of true positives (correctly identifying children at high risk of hospitalisation and appropriately referring them on for secondary care assessment and potential admission), true negatives (correctly identifying children at low risk of hospitalisation and being reassured that they can be cared for at home), false positives (unnecessarily referring children to secondary care that do not require it and potentially overburdening services), and false negatives (failing to identify children that require hospital level care and the potential for them to deteriorate).

The committee agreed that good specificity was important as it would help clinicians to identify children at low or very low risk of hospitalisation and provide reassurance that those children could be safely treated at home. This would also help to avoid over-referral to secondary care. However, they agreed that false negatives could be particularly impactful because they could lead to treatment being delayed and a potential worsening of the child's condition, hence a particular need to focus on test sensitivity. They noted that in practice, it can be difficult to identify the small number of very unwell children at most risk from the much larger number of children with a respiratory infection that can be safely treated at home, particularly at first presentation in primary care. They therefore agreed that sensitivity and specificity were both of interest when considering the accuracy of risk assessment tools for predicting the need for hospitalisation.

The committee also considered positive and negative likelihood ratios, where reported, alongside sensitivity and specificity to help them interpret and understand the meaning of the risk prediction tool result: a positive test increases the likelihood of the patient requiring referral to secondary care, and a negative test decreases it.

1.1.12.2 The quality of the evidence

The studies were assessed for risk of bias; 2 were rated as being at low risk of bias and 2 were rated as being at moderate risk of bias. The 2 studies at moderate risk were based on the same sample and study methodology, so the reasons for downgrading were the same: predominantly because the method of outcome assessment was unclear and appeared to rely on self-report by caregivers; hospital records were not obtained to confirm hospital admission.

Where possible, the quality of the evidence was assessed using GRADE and was rated as low to very low quality for all outcomes that could be GRADED. Evidence was largely downgraded due to indirectness or inconsistency (single study outcomes were downgraded once for inconsistency and all outcomes in this review were from single studies only). The quality of some outcomes could not be assessed using GRADE because confidence intervals were not reported, or because there is no established method for applying GRADE to data on risk percentages (reported in Hay 2016 and Wilde 2021). In these instances, the risk of bias judgement and applicability of the included study was reported. No meta-analyses were conducted for any of the prediction models because of the high level of heterogeneity between studies in terms of the prediction models used, the outcomes reported, and the study populations.

The committee discussed the applicability of the Gallagher 2021 and Wildes 2021 studies, which were 2 publications based on the same population of children with CAP attending primary care facilities in Malawi. They noted the rate of immunisation was quite high for this region and the organisms identified were similar to those you would expect to find in the UK. Although there were higher rates of HIV (2%) and malaria (19%) in this population than would be seen in UK populations, there were no significant differences in the rates of these conditions between the hospitalised and non-hospitalised children. The trial was conducted in an urban area in Northern Malawi with access to secondary care, rather than more rural areas where hospital admission may not be an option, so there was a degree of applicability to UK settings. However, the committee noted that some aspects of primary care in Malawi may be delivered by non-doctor trained physician associates and overall, the structure and delivery of the healthcare system and approach to hospital admission is not sufficiently applicable to UK healthcare settings. They agreed that they were not able to make recommendations based on the results of this study.

The committee considered the study populations in Bos 2023 and Hay 2016. They noted the young age of the samples (under 5 years) relative to the protocol (under 18 years), but the committee noted that this was representative of the majority of patients seen in primary care for lower respiratory tract infections (LRTI): predominantly under 5s, so they were not concerned about the applicability of these study samples. They highlighted that they were more likely to need a tool to support decision making for this age group because they are less able to articulate how they are feeling, relative to older children.

The committee discussed the Bos 2023 study and noted that a large proportion of the children admitted to hospital came from the sub-population recruited in emergency departments. The overall study population was primarily recruited in primary care settings

(from 98 GP and outpatient practices, and from 6 ED settings), but the large majority of serious infections requiring hospital admission were diagnosed in patients seen in the ED: of the 498 patients hospitalised, 23 were from a GP setting, 109 were from an ambulatory paediatrician, and 366 were from ED. Separate analyses by admission setting were not reported. This raised concerns about the applicability of the data and the accuracy of the tools for predicting hospitalisation in children attending primary care.

The committee considered the proportion of pneumonia patients in each of the samples, noting that they were very low (<2%), with most children being diagnosed with other respiratory illnesses. They acknowledged that this was representative of the prevalence of pneumonia diagnoses in UK primary care but expressed concern about the relevance of these tools to pneumonia patients, since they are primarily based on samples of children with acute cough. They were concerned that the evidence reviewed was based on children with undifferentiated respiratory illness and not pneumonia, meaning that the findings were not specific enough to be applied to a pneumonia guideline.

The committee noted that 3 of the 4 studies reported on hospital admission within 30 days rather than immediate referral, suggesting that the tools were primarily predicting future need for hospitalisation rather than identifying the children who needed direct referral to hospital from the primary care consultation for further assessment and treatment (e.g. oxygen, IV fluids, IV antibiotics or more intensive monitoring). In both Hay 2016 and Wildes 2021, only 19% of children were admitted to hospital on the day of recruitment, and in Hay 2016, 24% were admitted between days 15 and 30. The committee recognised that these tools may help to identify those children who deteriorate in the days and weeks following assessment and require subsequent hospitalisation, but there was concern that this evidence did not directly answer the clinical question about which tools would support in-consultation decision making for children who need referring for secondary care assessment.

1.1.12.3 Benefits and harms

The evidence showed that all the models performed comparatively well in terms of c-statistics, with all models showing good to excellent classification accuracy. Similarly, all 4 models were considered ‘a moderately useful test’ for identifying children at risk of hospitalisation for pneumonia based on sensitivity and specificity values, but this varied with the risk thresholds used. The committee noted that none of the models were shown to be both very sensitive and very specific, and when they were in the range of ‘a good test’ for specificity (≥90%), the sensitivity values fell into the ‘not a useful test’ range (<50%).

The committee considered the risk prediction models presented in the evidence and noted that the Feverkidstool and the Craig model were both tools originally designed for use in emergency departments for predicting the presence of serious bacterial infections in febrile children. Although the Bos 2023 study validated these tools for use in primary care and reported model performance for pneumonia, making them relevant for this review, the committee highlighted that they are still more suited for use in EDs due to their comprehensive assessment process (10 items and 26 items, respectively), the inclusion of items not specific to pneumonia due to their primary function of predicting all serious bacterial infections, and their need for a computer program to calculate the overall score and generate a specific risk category using a complex algorithm. They agreed that this would not be practical during a short primary care consultation. They also noted that the Feverkidstool requires a CRP measurement, which is not available in all primary care settings and would be difficult to implement. For these reasons, the committee did not consider it appropriate to make recommendations about the Feverkidstool or the Craig model.

The committee discussed the STARWAVe tool and agreed that it was the most applicable to primary care given that it was a simple tool comprising a small number of items that are routinely collected during a consultation with a child presenting with LRTI symptoms and was developed in primary care. They noted that it was primarily developed to support antibiotic prescribing decisions, particularly to give confidence to clinicians to not prescribe antibiotics for children in the very low risk group, but had been used in some settings to identify children at risk of hospitalisation. The sensitivity and specificity data showed the test performed moderately well when using a threshold of very low risk vs. normal or high risk, but when using a threshold of high risk vs. normal or very low risk, the test was very specific but showed very low sensitivity. This indicates that it is good at identifying children with a low risk of hospital admission, but poor at identifying children at high risk of hospital admission.

The committee considered the data on risk of admission and STARWAVe scores for hospitalised and non-hospitalised children reported in Hay 2016. The data showed that the risk of hospital admission increased as the STARWAVe score increased, and that children scoring in the very low risk range (scores of 0 or 1) had a lower risk percentage (0.3%) of hospital admission than the overall population (0.9%), suggesting that children in the very low risk group were very unlikely to need hospital admission. Similarly, 31% of hospitalised children were in the high-risk group (scores of ≥4), compared to only 2% of children in the non-hospitalised group. However, the data also showed that 47% of the hospitalised children had a STARWAVe score of 2 to 3, putting them in the normal risk group. Furthermore, 22% of the hospitalised children were in the very low risk group, suggesting that these children would not have been considered as requiring hospitalisation based on the STARWAVe criteria.

There was some committee discussion on the potential usefulness of the STARWAVe tool in primary care, noting that the system is lacking a tool that provides clear guidance on how to identify children with suspected pneumonia most at risk of deteriorating. They highlighted the high demand placed on primary care by the volume of children presenting with LRTI symptoms, and the challenge of identifying 'the abnormal in a sea of normal.' They suggested that the STARWAVe tool could be used as a guide to more confidently identify those children where there are concerns about illness progression. However, it was agreed that overall the evidence was not strong enough or specific enough to pneumonia to recommend using STARWAVe at this time and for this use. The evidence indicated that the tool was better able to identify children at lowest risk of deterioration where a need for hospital admission could be confidently ruled out, rather than accurately identifying children at highest risk of hospitalisation who require onward referral, so it may not be able to perform in the way most needed in primary care. In addition, there were concerns about its relevance in a pneumonia guideline, since it has only been derived and internally validated in a population of children with acute cough, of which a very small proportion (<1%) had a final diagnosis of pneumonia. They agreed that it has potential as a tool for guiding patient management decisions in broader populations of children with acute cough and other LRTI symptoms, but not for pneumonia. Furthermore, the Hay 2016 study reports on derivation and internal validation only, so external validation would be required to test model performance in a different cohort before it can be recommended for use.

The committee concluded that they did not find the evidence sufficiently comprehensive or compelling to recommend any of the tools reviewed for use in children with suspected pneumonia, so they did not make any recommendations for this review question. The committee did make a research recommendation as they acknowledged that it's important for primary care physicians to have a reliable assessment tool to identify children who are most at high risk of future deterioration and who need referral to secondary care.

1.1.12.4 Cost effectiveness and resource use

There was no existing health economic evidence for this review question. While the use of a prediction tool is unlikely to have a resource impact the results of the tool may do. The committee were aware that if they recommended a prediction tool that was overly cautious and unnecessarily send people to hospital, this would potentially have a large resource impact. Given the clinical evidence the committee did not feel that they could make any recommendations. Therefore, there will not be a resource impact.

1.1.12.5 Other factors the committee took into account

The committee discussed other NICE guidance in this area, particularly the Fever in under 5s: Assessment and initial management guideline and the NICE Traffic Light System contained within that guideline. They noted that the Traffic Light System is widely used in primary care when evaluating febrile children but reported some concerns with the usability of this tool, such as that it can overestimate a child's risk level and lead to over referral of children to secondary care. It is also not designed specifically for use in children with suspected pneumonia. They acknowledged a need for more simplified, user-friendly tools to support primary care practitioners to confidently make decisions about which children may benefit from secondary care assessment.

1.1.13 Recommendations supported by this evidence review

No recommendations were made from this evidence review.

1.1.14 References – included studies

1.1.14.1 Prognostic

Bos, David A G, De Burghgraeve, Tine, De Sutter, An et al. (2023) Clinical prediction models for serious infections in children: external validation in ambulatory care. BMC medicine 21(1): 151

Gallagher, Joe, Chisale, Master, Das, Sudipto et al. (2021) Aetiology and severity of childhood pneumonia in primary care in Malawi: a cohort study. BMJ open 11(7): e046633

Hay, Alastair D, Redmond, Niamh M, Turnbull, Sophie et al. (2016) Development and internal validation of a clinical rule to improve antibiotic use in children presenting to primary care with acute respiratory tract infection and cough: a prognostic cohort study. The Lancet. Respiratory medicine 4(11): 902-910

Wildes, Dermot M, Chisale, Master, Drew, Richard J et al. (2021) A Systematic Review of Clinical Prediction Rules to Predict Hospitalisation in Children with Lower Respiratory Infection in Primary Care and their Validation in a New Cohort. EClinicalMedicine 41: 101164

1.1.14.2 Economic

No included studies

1.1.14.3 Other

Craig JC, Williams GJ, Jones M, Codarini M, Macaskill P, Hayen A, et al. The accuracy of clinical symptoms and signs for the diagnosis of serious bacterial infection in young febrile children: prospective cohort study of 15 781 febrile illnesses. BMJ (Online). 2010;340:1015.

Nijman RG, Vergouwe Y, Thompson M, van Veen M, van Meurs AHJ, van der Lei J, et al. Clinical prediction model to aid emergency doctors managing febrile children at risk of serious bacterial infections: diagnostic study. BMJ (Online). 2013;346:1–16.

Appendices

Appendix A – Review protocols

Review protocol for RQ1.1: In babies, children and young people with suspected community-acquired pneumonia who present to primary care, what is the most accurate and cost-effective outcome prediction tool to identify under 18s whose outcome will be improved by referral to hospital?

ID	Field	Content
1.	Review title	The usefulness of prediction tools to identify babies, children or young people in primary care who would benefit from referral to hospital.
2.	Review question	In babies, children and young people with suspected community-acquired pneumonia who present to primary care, what is the most accurate and cost-effective outcome prediction tool to identify under 18s whose outcome would be likely to benefit by referral to hospital?
3.	Objective	To evaluate the predictive accuracy of prediction tools for determining which children with suspected community-acquired pneumonia would benefit from hospital care.

4.	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 evidence specific to this review question. **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]). **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. **Searches specific to this review question**

		The searches for 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 records potentially relevant to the parameters set out in sections 6-10 below are not missed the following will be checked as required: • The reference lists of any appropriate studies identified from the combined systematic reviews search covering all questions in this guideline. • Later citations of any key trials, reviews or protocols identified in the combined systematic reviews search, scoping searches for this guideline, evidence reviews for previous NICE guidelines or the searches specific to this review question. 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 not include any date limits. **Managing all search results** Database functionality will be used, where available, to exclude from all searches: • Animal studies • Editorials, letters, news items and commentaries • Conference abstracts and posters • 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.

5.	Condition or domain being studied	Community-acquired pneumonia
6.	Population	Inclusion: Babies over 28 days (corrected gestational age), children, young people (age <18 years) with suspected community-acquired pneumonia presenting to primary care. • CAP is defined as pneumonia that is acquired outside hospital We will prioritise studies including pneumonia patients only (or where >75% of the sample have pneumonia), but if insufficient studies on pneumonia-only patients are identified (too low quantity or quality to support decision making), we will consider the inclusion of studies of children with suspected lower respiratory tract infection (LRTI). Studies of LRTI patients will be downgraded for indirectness, and the committee will be asked to extrapolate from this evidence to pneumonia patients. Exclusion: • Babies up to and including 28 days (corrected gestational age). • People with hospital-acquired pneumonia. • 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.
7.	Prognostic tool of interest	Tools that use a collection of respiratory and fever based symptoms or prediction model based on a collection of symptoms. **Prediction tools** • Starwave • Feverkidstool • Prediction models based on symptoms Individual symptoms predictive of hospital admission will not be included unless part of a risk prediction model.

8.	Outcomes to be predicted	• Admission to hospital • Admission to ICU • Admission to acute respiratory unit • Length of stay (in any of the above settings) • Primary care re-attendance with CAP (as a marker of failure of original decision) **Effect/performance measures of interest:** Discrimination measures: • Concordance (C) statistic, area under the curve (AUC) with 95% confidence interval Calibration measures: • number of observed (O) and expected (E) events • total O:E ratio • calibration slope Where available the following measures will be reported: • adjusted hazard ratios (HR), adjusted odds ratios (OR) or adjusted risk ratios (RR).
9.	Types of study to be included	• Prospective or retrospective observational cohorts or cross-sectional studies which evaluate the performance of the risk prediction tools. These studies should include a multivariate analysis which accounts for key confounders. Key confounders will vary based on each risk factor but should at least include age and sex. • Validation studies

		• Systematic reviews of the above study types Case-control studies, derivation and internal validation studies will be excluded.
10.	Other exclusion criteria	None
11.	Context	It is important to identify the clinical symptoms and physical examination findings associated with pneumonia to improve timely diagnosis, prevent significant morbidity, and limit antibiotic overuse.
13.	Secondary outcomes (important outcomes)	None
14.	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 section 6.4). Study investigators may be contacted for missing data where time and resources allow. The priority screening functionality within the EPPI-reviewer software will not be used for this review.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. These may include: • Risk of Bias in Systematic Reviews (ROBIS) for systematic reviews • PROBAST for risk prediction modelling for a prognosis • QUIPS for any association studies
16.	Strategy for data synthesis	**Approach to meta-analysis** Where appropriate, C statistic data and O:E ratios will be meta-analysed (separately) using Cochrane Review Manager (RevMan5). Summary statistics will be reported from the meta-analyses with their 95% confidence intervals in forests plots and adapted GRADE tables.

		For the ROC data, the thresholds for indicating whether a test has good discrimination will be as follows: >0.50 - 0.60 indicates a very poor test >0.61-0.70 indicates a poor test >0.71- 0.80 indicates a moderate test >0.81 to 0.92 indicates a very good test and >0.92 to 1.00 indicates an excellent test Where appropriate, hazard ratios will be pooled using the generic inverse-variance method. Adjusted odds ratios, hazard ratios and risk ratios from multivariate models will only be pooled if the same set of factors are used across multiple studies and if the same thresholds to measure factors were used across studies. Where data can be disambiguated it will be separated into the subgroups identified in section 17 (below). 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 outcomes, 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 $I^2 \geq 50\%$. Random effects meta-analysis will be used when the I^2 is 50% or greater. **Approach to GRADE** A modified approach will be applied using the GRADE framework.

		Evidence from cohorts will initially be rated as high-quality, and then assessed according to the same criteria as described in the standard GRADE criteria (risk of bias, inconsistency, imprecision and indirectness).
17.	Analysis of sub-groups	The following groups will be considered separately if data are available: • Age: 0-1; 1-5; 5-18 or other age groups defined by the studies
18.	Type and method of review	☐ Intervention ☐ Diagnostic ☒ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
19.	Language	English
20.	Country	England

21.	Anticipated or actual start date	TBC		
22.	Anticipated completion date	TBC		
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☐	☐
		Piloting of the study selection process	☐	☐
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐

		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	**5a. Named contact** Guideline Development Team B, Centre for Guidelines, NICE. **5b Named contact e-mail** pneumoniadev@nice.org.uk **5c Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE)		
25.	Review team members	From the Centre for Guidelines: • Chris Carmona, Technical Adviser • Robby Richey, Topic Lead • Hannah Stockton, Technical Analyst • Michellie Young, Technical Analyst • Rachel Walsh, Technical Analyst • Steph Armstrong, Health Economist • Eric Slade, Health Economic Advisor		

		• Paul Levay, Information specialist • Christine Harris, Project Manager • Adam O'Keefe, Project Manager
26.	Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the

		guideline committee are available on the NICE website: : Project information | Pneumonia: diagnosis and management (update) | Guidance | NICE
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	Pneumonia, community acquired infections, signs and symptoms, diagnosis, diagnostic accuracy.

33.	Details of existing review of same topic by same authors	None
34.	Current review status	☐ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	
36.	Details of final publication	www.nice.org.uk

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 prognostic evidence searches.

- Part 2: Evidence searches

This search was developed separately and tailored to each evidence review. For this review, it was further divided into Part 2A covering named outcome prediction tools and Part 2B covering other tools. The searches for Effectiveness evidence (Part 2) were run on 24 September 2024.

- 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. 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. All translated search strategies were peer reviewed by another SIS to ensure their accuracy. The QA 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).

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 countries

For the Cost Effectiveness (Part 3) searches, the validated NICE OECD filters were used in MEDLINE and Embase to remove references 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.

> 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.

No date limits were applied to the Effectiveness searches (Part 2) as these were new questions.

Study-type filters

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

The searches for Part 2A had no filters as there was a very small number of results on the two tools named in the protocol.

The searches for Part 2B applied standard NICE filters for cohort, cross-sectional and validation studies. Systematic reviews were not included as these had already been covered in the Part 1 searches. The cohort studies filter followed standard NICE practice e.g. they have been used in Tobacco NG209 (Review J: NRT in pregnancy) in March 2019, Gambling-related harms (NG248) (Review A: Factors) in November 2022 and other reviews for this guideline. They were originally based on the BMJ MEDLINE cohort study strategy from the BMJ Best Practice Evidence-based medicine (EBM) toolkit and from reviewing the terms used by Waffenschmidt et al.

> Waffenschmidt S et al. (2020) Development and validation of study filters for identifying controlled non-randomized studies in PubMed and Ovid MEDLINE. *Research Synthesis Methods*, 11(5): 617-626.

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.

As this search was only covering tools used in primary care the Emtree term hospital acquired pneumonia/ was removed for Part 2B.

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

Part 2: Evidence searches

The search results from Parts 2A and 2B were screened in a single EPPI-Reviewer file after duplicates from across the searches had been removed. The same limits were applied to both searches. They were done separately so that broad searches for the tools named in the protocol could be done without applying terms for young people, primary care or study filters. This was feasible as there were only 40 results from MEDLINE, Embase and CENTRAL. The MEDLINE search for other tools for Part 2B had over 233,000 results without these other sets of terms.

The strategies are in the structure:

- Part 2A: (STARWAVe OR Feverkidstool) AND Limits
- Part 2B: ((Pneumonia OR LRTI OR Respiratory Symptoms) AND Prediction Tools AND Primary care AND Children AND (Cohorts OR Cross sectional OR Validation) AND Limits

As this search was covering "suspected pneumonia" and the search terms were expanded to cover suspected lower respiratory tract infection (LRTI) and associated symptoms. The terms for LRTI were written after referring to question F.1.3 in the searches for CG191 (March 2014) and Suspected acute respiratory infection in over 16s: assessment at first presentation and initial management (NICE guideline NG237) (September 2023), as well as Deardorff et al. Pneumonia risk stratification scores for children in low-resource settings: a systematic literature review (2018) and Wildes et al. A systematic review of clinical prediction rules to predict hospitalisation in children with lower respiratory infection in primary care and their validation in a new cohort (2021). As the GP would not have made a diagnosis, and the LRTI was suspected, it was important to also include respiratory symptoms. The list of LRTIs was derived from the advice received from the clinical adviser during the scoping searches to include illnesses that predominantly affect the respiratory tree below the larynx. This was why the narrower terms were picked rather than exploding the

MeSH term "Respiratory Tract Infections". The MEDLINE search with 2217 results would have had 400 results with just the standard pneumonia search terms.

The terms in Part 2B to describe outcome prediction tools were partly derived from examining the test set in Yale MeSH Analyzer on 17/9/24. For details of the test set see the seed references in the table below 'Forward citation searching and reference list checking (Parts 2A and 2B)'.

The Emtree terms for outcome prediction tools were all focussed. This reduced the search from 3556 to 2127 results. A sample of the papers that would be missed was reviewed and none were relevant to this protocol. The risk of missing a relevant paper was minimal as it would have to be: not retrieved or unavailable from MEDLINE or CENTRAL; not have any relevant free-text terms; and not be indexed with a focussed Emtree heading. This helped to focus the search on papers about the tools, rather than papers that referred to use of the tools in a wider study.

The terms for children and young people were based on those used in an earlier review for this guideline (Corticosteroids for treating pneumonia in children search Part 2C), except terms for hospitalized children were removed from Emtree i.e. hospitalized child/ or hospitalized infant/ or hospitalized adolescent/ or pediatric hospital/ or pediatric ward/ or pediatric intensive care unit/.

The primary care terms were written after consulting a validated filter from Brown et al. This filter is for PubMed so it was adapted for Ovid MEDLINE ALL and some updates made: removed the explode from Primary Health Care/, Physicians Primary Care/ and General Practitioners/ (as there are no narrower terms); removed Family Practice/ as it was already retrieved by exp General Practice/; and did not include the terms relating to community pharmacy.

Brown L et al. (2014) Facilitating access to evidence: Primary Health Care Search Filter. *Health Information and Libraries Journal*, 31(4), 293-302.

The additional search techniques, forward citation searching and reference list checking, were done separately but they covered both Parts 2A and 2B at the same time, as the seed references were relevant to both parts.

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
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*))

Searches
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"))
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

Searches
"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 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 2: Evidence searches

Database results – Part 2A (named outcome prediction tools)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	24/9/24	Wiley	Cochrane Central Register of Controlled Trials Issue 8 of 12, August 2024	8

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Embase	24/9/24	Ovid	Embase 1974 to 2024 September 23	17
MEDLINE ALL	24/9/24	Ovid	Ovid MEDLINE(R) ALL 1946 to September 23, 2024	15

Database results – Part 2B (other outcome prediction tools)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	24/9/24	Wiley	Cochrane Central Register of Controlled Trials Issue 8 of 12, August 2024	456
Embase	24/9/24	Ovid	Embase 1974 to 2024 September 23	2127
MEDLINE ALL	24/9/24	Ovid	Ovid MEDLINE(R) ALL 1946 to September 23, 2024	2217

Additional search techniques – Parts 2A and 2B

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	19/9/24	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-09-16	254
Reference list checking	19/9/24	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-09-16	219

Search strategy history

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

Searches – Part 2A
#1 STARWAVe*:ti,ab 8
#2 (Short illness NEAR/3 Temperature NEAR/3 Age NEAR/3 Recession NEAR/3 Wheeze NEAR/3 Asthma NEAR/3 Vomiting):ti,ab 4
#3 (Feverkidstool* or Feverkids-tool* or Fever-kids-tool*):ti,ab 1
#4 {or #1-#3} 9
#5 ((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 534051
#6 #4 not #5 8
#7 "conference":pt 247486
#8 #6 not #7 8
#9 #6 not #7 in Trials 8

Searches – Part 2B
#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"] 4465
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 16255
#3 #1 or #2 17503
#4 [mh ^"Respiratory Tract Infections"] 3087
#5 [mh ^"Pneumovirus Infections"] or [mh ^"Respiratory Syncytial Virus Infections"] or [mh ^Bronchitis] or [mh ^Bronchiolitis] or [mh ^"Bronchiolitis, Viral"] or [mh ^Bronchiectasis] or [mh ^Tracheitis] or [mh ^"Whooping Cough"] or [mh "Legionellosis"] or [mh ^"Empyema, Pleural"] or [mh ^"Lung Abscess"] or [mh ^Pleurisy] or [mh ^"Tuberculosis, Pulmonary"] or [mh ^"Severe Acute Respiratory Syndrome"] or [mh ^"COVID-19"] 13120
#6 ((acute* or low*) NEAR/1 ((respirat* NEXT tract*) or airway*) NEAR/3 (infect* or illness* or inflam* or disease*)):ti,ab 2025
#7 (Pneumovirus* or Bronchitis* or Bronchiolitis* or Bronchiectasis* or Tracheobronchitis* or Tracheitis* or Whooping* or pertussis* or pertusses* or coronavirus* or "severe acute respiratory syndrome" or SARS or COVID*):ti,ab 30253
#8 ((pulmonary* or lung* or airway* or airflow* or bronch* or respirat*) NEAR/2 (syncytial NEXT virus*)):ti,ab 1122
#9 [mh ^Cough] or [mh ^Sputum] or [mh ^Hemoptysis] or [mh ^"Pleural Effusion"] or [mh ^Dyspnea] or [mh ^Fever] or [mh ^"Chest Pain"] or [mh ^Tachypnea] or [mh ^Cyanosis] or [mh ^"Oxygen Saturation"] or [mh ^Hypoxia] or [mh ^"Respiratory Sounds"] 12430
#10 (sputum* or phlegm* or mucopurulent* or purulent* or purulence* or hemoptysis* or haemoptysis* or dyspnoea* or dyspnea* or breathless* or fever* or febrile* or pyrexia* or tachypnea* or tachyponea* or cyanosis* or cyanoses* or Hypoxia* or hypoxemia* or rale or rales* or crepitation* or rhonchi* or rhoncus* or stridor* or wheeze* or wheezing*):ti,ab 54917

Searches – Part 2B
#11 ((acute* or subacute* or exacerbat* or prolong*) NEAR/3 cough*):ti,ab 473
#12 ((lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or chest* or broncho* or tracheo* or thorax* or thoracic*) NEAR/3 (infect* or inflam* or abscess* or coinfect* or consolidat* or recession* or pain* or ache* or aching* or effusion* or empyema*)):ti,ab 13301
#13 ((respirat* or lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or breathing*) NEAR/2 (crackle* or noise* or sound*)):ti,ab 226
#14 ((labour* or labor* or heavy* or abnormal* or unusual* or rapid* or fast* or slow* or difficult* or shortness*) NEAR/2 (breath* or respiration*)):ti,ab 4179
#15 (oxygen* NEAR/2 (saturat* or deficien*)):ti,ab 15277
#16 ((acute* or exacerbat* or flare*) NEAR/3 (copd or coad or ("chronic obstructive pulmonary" NEXT disease*) or ("chronic obstructive" NEXT airway* NEXT disease*) or ("chronic obstructive lung" NEXT disease*))):ti,ab 4451
#17 ((lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or chest* or broncho* or tracheo*) NEAR/3 (Tuberculosis* or TB or (Common NEXT Cold*) or Influenza* or flu or Legionellosis* or Legionnaire* or Pleurisy* or croup*)):ti,ab 2654
#18 (LRTI or ARTI or LRI or ALRI or RTI or RSVI or RSV or AECOPD or AEBX):ti,ab 3070
#19 {or #4-#18} 115934
#20 #3 or #19 125452
#21 [mh ^"Severity of Illness Index"] 25739
#22 [mh ^"health status indicators"] 1230
#23 [mh ^"Surveys and Questionnaires"] 36669
#24 [mh ^"risk assessment"] or [mh ^"risk management"] 13767
#25 [mh ^"Symptom Assessment"] 454
#26 [mh ^"Models, Statistical"] 2277
#27 [mh ^"Disease Progression"] or [mh ^"Clinical Deterioration"] 10418
#28 [mh ^"Clinical Decision-Making"] or [mh ^"Clinical decision rules"] or [mh ^"Decision Support Techniques"] 2110
#29 (predict* NEAR/3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify* or risk* or outcome* or clinical* or hospitalis* or hospitaliz* or deteriorat* or severity* or severe* or progress* or decision* or mortality* or death* or morbidity*)):ti,ab 36638
#30 ((outcome* or clinical* or decision* or determin*) NEAR/3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model*)):ti,ab 244768
#31 (risk* NEAR/3 (detect* or identif* or manag* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify* or hospitalis* or hospitaliz* or deteriorat* or severity* or severe* or progress* or mortality* or death* or morbidity*)):ti,ab 57905
#32 ((severe* or severity*) NEAR/3 (detect* or identif* or define* or defining* or definition* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or

Searches – Part 2B
indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify*)):ti,ab45368
#33 (symptom* NEAR/3 (coalition* or cluster* or group* or collection* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify*)):ti,ab 64641
#34 (statistical* NEAR/3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or algorithm* or rating* or framework* or model*)):ti,ab 8493
#35 ((score* or scoring*) NEAR/3 (system* or criteria* or criterion* or rule* or ruling* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or algorithm* or rating* or framework* or model*)):ti,ab 50625
#36 ((disease* or illness* or clinical* or identif* or detect* or alert*) NEAR/3 (deteriorat* or progress* or exacerbat*)):ti,ab 38294
#37 {or #21-#36} 492294
#38 #20 and #37 36391
#39 [mh ^"primary health care"] 6629
#40 [mh "general practice"] 3153
#41 [mh ^"physicians, primary care"] 247
#42 [mh ^"general practitioners"] 605
#43 [mh ^"Practice Patterns, Physicians'"] 2039
#44 (primary* NEAR/2 (care* or healthcare*)):ti,ab 31021
#45 ((general* or family*) NEAR/2 (practice* or practitioner* or physician* or doctor* or medicine*)):ti,ab 16892
#46 GP:ti,ab 7388
#47 [mh ^"ambulatory care"] 3918
#48 [mh ^"ambulatory care facilities"] 805
#49 [mh ^"community health services"] 1383
#50 [mh ^"Community Health Workers"] 827
#51 [mh "Community Health Nursing"] 398
#52 [mh ^"home care services"] or [mh ^"Home Health Nursing"] or [mh ^"Home Nursing"] 2704
#53 [mh ^"House calls"] 760
#54 [mh ^"Outpatient Clinics, Hospital"] 642
#55 ((ambulatory* or outpatient*) NEAR/3 (care* or healthcare* or facility* or facilities* or clinic or clinics or department* or service* or setting*)):ti,ab 22155
#56 ((community* or communities* or neighbourhood* or neighborhood*) NEAR/2 (health* or care*) NEAR/2 (practice* or practitioner* or physician* or doctor* or medicine* or nurs* or worker* or professional* or facility* or facilities* or clinic or clinics or auxiliar*)):ti,ab 3113
#57 ((home* or house*) NEAR/1 (call* or visit* or care* or healthcare* or nurs*)):ti,ab 13345
#58 {or #39-#57} 87473
#59 #38 and #58 2917
#60 [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] 95890

Searches – Part 2B
#61 (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 245568
#62 [mh ^Adolescent] or [mh ^"Adolescent Behavior"] or [mh ^"Adolescent Health"] or [mh ^Puberty] 138259
#63 ((under NEXT 18*) or (under NEXT eighteen*)):ti,ab 17036
#64 (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 53661
#65 (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 30765
#66 {or #60-#65} 405302
#67 #59 and #66 902
#68 ((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 534051
#69 #67 not #68 555
#70 "conference":pt 247486
#71 #69 not #70 514
#72 #69 not #70 in Trials 456

Database name: Embase

Searches – Part 2A
1 STARWAVe*.ti,ab. 10
2 (Short illness adj3 Temperature adj3 Age adj3 Recession adj3 Wheeze adj3 Asthma adj3 Vomiting).ti,ab. 3
3 (Feverkidstool* or Feverkids-tool* or Fever-kids-tool*).ti,ab. 11
4 or/1-3 21
5 nonhuman/ not human/ 5536033
6 4 not 5 21
7 limit 6 to english language 21
8 (letter or editorial).pt. 2166384
9 7 not 8 21
10 Case report/ 3045152
11 9 not 10 21
12 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6031646
13 11 not 12 17

Searches – Part 2B
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

Searches – Part 2B
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/ 329570
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 247211
3 1 or 2 417737
4 respiratory tract infection/ or lower respiratory tract infection/ or chest infection/ or lung infection/ 125976
5 pneumovirus infection/ or exp respiratory syncytial virus infection/ or bronchitis/ or tracheobronchitis/ or bronchiolitis/ or viral bronchiolitis/ or bronchiectasis/ or tracheitis/ or pertussis/ or exp legionellosis/ or exp pleura empyema/ or lung abscess/ or pleurisy/ or lung tuberculosis/ or severe acute respiratory syndrome/ or coronavirus disease 2019/ or covid-19 pneumonia/ 606683
6 ((acute* or low*) adj1 (respirat* tract* or airway*) adj3 (infect* or illness* or inflam* or disease*)).ti,ab. 19710
7 (Pneumovirus* or Bronchitis* or Bronchiolitis* or Bronchiectasis* or Tracheobronchitis* or Tracheitis* or Whooping* or pertussis* or pertusses* or coronavirus* or "severe acute respiratory syndrome*" or SARS or COVID*2).ti,ab. 622276
8 ((pulmonary* or lung* or airway* or airflow* or bronch* or respirat*) adj2 syncytial virus*).ti,ab. 21973
9 coughing/ or sputum/ or hemoptysis/ or pleura effusion/ or dyspnea/ or fever/ or thorax pain/ or tachypnea/ or cyanosis/ or oxygen saturation/ or hypoxia/ or exp abnormal respiratory sound/ 1043040
10 (sputum* or phlegm* or mucopurulent* or purulent* or purulence* or hemoptysis* or haemoptysis* or dyspnoea* or dyspnea* or breathless* or fever* or febrile* or pyrexia* or tachypnea* or tachyponea* or cyanosis* or cyanoses* or Hypoxia* or hypoxemia* or rale or rales* or crepitation* or rhonchi* or rhoncus* or stridor* or wheeze* or wheezing*).ti,ab. 810249
11 ((acute* or subacute* or exacerbat* or prolong*) adj3 cough*).ti,ab. 2720
12 ((lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or chest* or broncho* or tracheo* or thorax* or thoracic*) adj3 (infect* or inflam* or abscess* or coinfect* or consolidat* or recession* or pain* or ache* or aching* or effusion* or empyema*)).ti,ab. 254259
13 ((respirat* or lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or breathing*) adj2 (crackle* or noise* or sound*)).ti,ab. 4171
14 ((labour* or labor* or heavy* or abnormal* or unusual* or rapid* or fast* or slow* or difficult* or shortness*) adj2 (breath* or respiration*)).ti,ab. 44681
15 (oxygen* adj2 (saturat* or deficien*)).ti,ab. 60642
16 ((acute* or exacerbat* or flare*) adj3 (copd or coad or "chronic obstructive pulmonary disease*" or "chronic obstructive airway* disease*" or "chronic obstructive lung disease*")).ti,ab. 20866
17 ((lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or chest* or broncho* or tracheo*) adj3 (Tuberculosis* or TB or Common Cold* or Influenza* or flu or Legionellosis* or Legionnaire* or Pleurisy* or croup*)).ti,ab. 51112
18 (LRTI or ARTI or LRI or ALRI or RTI or RSVI or RSV or AECOPD or AEBX).ti,ab. 33716
19 or/4-18 2298464
20 3 or 19 2509585

Searches – Part 2B
21 *scoring system/ or *"severity of illness index"/ or *health status indicator/ 32844
22 *questionnaire/ 47247
23 *risk model/ or *risk assessment/ or *health risk assessment/ or *risk management/ 101710
24 *symptom assessment/ 1875
25 *statistical model/ 26359
26 *disease exacerbation/ or *deterioration/ or *disease severity/ 69303
27 *clinical decision making/ or *clinical decision rule/ or *decision support system/ or *clinical decision support system/ 25239
28 (predict* adj3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify* or risk* or outcome* or clinical* or hospitalis* or hospitaliz* or deteriorat* or severity* or severe* or progress* or decision* or mortality* or death* or morbidity*)).ti,ab. 897742
29 ((outcome* or clinical* or decision* or determin*) adj3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model*)).ti,ab. 1299894
30 (risk* adj3 (detect* or identif* or manag* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify* or hospitalis* or hospitaliz* or deteriorat* or severity* or severe* or progress* or mortality* or death* or morbidity*)).ti,ab. 1076988
31 ((severe* or severity*) adj3 (detect* or identif* or define* or defining* or definition* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify*)).ti,ab. 274989
32 (symptom* adj3 (coalition* or cluster* or group* or collection* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify*)).ti,ab. 250983
33 (statistical* adj3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or algorithm* or rating* or framework* or model*)).ti,ab. 95390
34 ((score* or scoring*) adj3 (system* or criteria* or criterion* or rule* or ruling* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or algorithm* or rating* or framework* or model*)).ti,ab. 265798
35 ((disease* or illness* or clinical* or identif* or detect* or alert*) adj3 (deteriorat* or progress* or exacerbat*)).ti,ab. 471090
36 or/21-35 3983065
37 20 and 36 360141
38 exp primary health care/ 222408
39 general practice/ 87942
40 general practitioner/ 125823
41 (primary* adj2 (care* or healthcare*)).ti,ab. 259649

Searches – Part 2B
42 ((general* or family*) adj2 (practice* or practitioner* or physician* or doctor* or medicine*)).ti,ab. 202777
43 GP.ti,ab. 77852
44 exp ambulatory care/ 55707
45 outpatient department/ 93241
46 health center/ 44563
47 community care/ 62690
48 health auxiliary/ 10620
49 Community Health Nursing/ 24444
50 home care/ or home respiratory care/ or home visit/ or visiting nursing service/ 78882
51 ((ambulatory* or outpatient*) adj3 (care* or healthcare* or facility* or facilities* or clinic or clinics or department* or service* or setting*)).ti,ab. 199740
52 ((community* or communities* or neighbourhood* or neighborhood*) adj2 (health* or care*) adj2 (practice* or practitioner* or physician* or doctor* or medicine* or nurs* or worker* or professional* or facility* or facilities* or clinic or clinics or auxiliar*)).ti,ab. 18397
53 ((home* or house*) adj1 (call* or visit* or care* or healthcare* or nurs*)).ti,ab. 98402
54 or/38-53 1068398
55 37 and 54 19983
56 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 child hospitalization/ 3392340
57 (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. 3464029
58 exp adolescent/ or adolescent behavior/ or adolescent health/ or exp Puberty/ 1911475
59 elementary student/ or high school student/ or middle school student/ 14096
60 ("under 18*" or "under eighteen*").ti,ab. 8367
61 (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. 812969
62 (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. 495107
63 or/56-62 5787272
64 55 and 63 4920
65 cohort analysis/ 1222687
66 longitudinal study/ 221826
67 prospective study/ 942231
68 retrospective study/ 1686844
69 follow up/ 2250529
70 ((follow up* or followup* or concurrent* or incidence* or population*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. 868317
71 (longitudinal* or prospective* or retrospective* or cohort*).ti,ab. 4438191
72 cross-sectional study/ 666623

Searches – Part 2B
73 ((prevalence* or disease frequenc*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. 102140
74 (crosssection* or crossection* or "cross section*").ti,ab. 817233
75 validation study/114967
76 external validity/ or predictive validity/ or validity/ 98136
77 predictive value/ 275242
78 Receiver operating characteristic/ 243300
79 prognosis/ or prognostic assessment/ 719969
80 ((valid* or concordance* or calibrat*) adj3 (external* or study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. 337776
81 (prognostic* adj3 (study* or studies* or analy* or observation* or design* or method* or research* or variable*)).ti,ab. 67796
82 (c-statistic* or "area under the curve" or AUC or "Receiver operating characteristic*" or ROC).ti,ab. 429245
83 or/65-82 8347735
84 64 and 83 2977
85 nonhuman/ not human/ 5536033
86 84 not 85 2974
87 limit 86 to english language 2906
88 (letter or editorial).pt. 2166384
89 87 not 88 2902
90 Case report/ 3045152
91 89 not 90 2789
92 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6031646
93 91 not 92 2127

Database name: MEDLINE ALL

Searches – Part 2A
1 STARWAVe*.ti,ab. 7
2 (Short illness adj3 Temperature adj3 Age adj3 Recession adj3 Wheeze adj3 Asthma adj3 Vomiting).ti,ab. 3
3 (Feverkidstool* or Feverkids-tool* or Fever-kids-tool*).ti,ab. 8
4 or/1-3 15
5 limit 4 to english language 15
6 limit 5 to (letter or historical article or comment or editorial or news or case reports) 0
7 5 not 6 15

Searches – Part 2B
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/ 126138

Searches – Part 2B
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 166701
3 1 or 2 236956
4 Respiratory Tract Infections/ 44205
5 Pneumovirus Infections/ or Respiratory Syncytial Virus Infections/ or Bronchitis/ or Bronchiolitis/ or Bronchiolitis, Viral/ or Bronchiectasis/ or Tracheitis/ or Whooping Cough/ or exp Legionellosis/ or Empyema, Pleural/ or Lung Abscess/ or Pleurisy/ or Tuberculosis, Pulmonary/ or Severe Acute Respiratory Syndrome/ or COVID-19/ 427280
6 ((acute* or low*) adj1 (respirat* tract* or airway*) adj3 (infect* or illness* or inflam* or disease*)).ti,ab. 13980
7 (Pneumovirus* or Bronchitis* or Bronchiolitis* or Bronchiectasis* or Tracheobronchitis* or Tracheitis* or Whooping* or pertussis* or pertusses* or coronavirus* or "severe acute respiratory syndrome*" or SARS or COVID*2).ti,ab. 527903
8 ((pulmonary* or lung* or airway* or airflow* or bronch* or respirat*) adj2 syncytial virus*).ti,ab. 17751
9 Cough/ or Sputum/ or Hemoptysis/ or Pleural Effusion/ or Dyspnea/ or Fever/ or Chest Pain/ or Tachypnea/ or Cyanosis/ or Oxygen Saturation/ or Hypoxia/ or Respiratory Sounds/ 233504
10 (sputum* or phlegm* or mucopurulent* or purulent* or purulence* or hemoptysis* or haemoptysis* or dyspnoea* or dyspnea* or breathless* or fever* or febrile* or pyrexia* or tachypnea* or tachyponea* or cyanosis* or cyanoses* or Hypoxia* or hypoxemia* or rale or rales* or crepitation* or rhonchi* or rhoncus* or stridor* or wheeze* or wheezing*).ti,ab. 555285
11 ((acute* or subacute* or exacerbat* or prolong*) adj3 cough*).ti,ab. 1676
12 ((lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or chest* or broncho* or tracheo* or thorax* or thoracic*) adj3 (infect* or inflam* or abscess* or coinfect* or consolidat* or recession* or pain* or ache* or aching* or effusion* or empyema*)).ti,ab. 158309
13 ((respirat* or lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or breathing*) adj2 (crackle* or noise* or sound*)).ti,ab. 2282
14 ((labour* or labor* or heavy* or abnormal* or unusual* or rapid* or fast* or slow* or difficult* or shortness*) adj2 (breath* or respiration*)).ti,ab. 21820
15 (oxygen* adj2 (saturat* or deficien*)).ti,ab. 40666
16 ((acute* or exacerbat* or flare*) adj3 (copd or coad or "chronic obstructive pulmonary disease*" or "chronic obstructive airway* disease*" or "chronic obstructive lung disease*")).ti,ab. 11165
17 ((lung* or lobar* or pulmonary* or pulmonic* or pulmonal* or pleura* or pleuritic* or pneumonic* or chest* or broncho* or tracheo*) adj3 (Tuberculosis* or TB or Common Cold* or Influenza* or flu or Legionellosis* or Legionnaire* or Pleurisy* or croup*)).ti,ab. 51062
18 (LRTI or ARTI or LRI or ALRI or RTI or RSVI or RSV or AECOPD or AEBX).ti,ab. 23949
19 or/4-18 1466498
20 3 or 19 1586450
21 "Severity of Illness Index"/ 276810
22 health status indicators/ 24142
23 "Surveys and Questionnaires"/ 595048
24 risk assessment/ or risk management/ 335317
25 Symptom Assessment/ 7159
26 Models, Statistical/ 100885

Searches – Part 2B
27 Disease Progression/ or Clinical Deterioration/ 197591
28 Clinical Decision-Making/ or Clinical decision rules/ or Decision Support Techniques/ 38227
29 (predict* adj3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify* or risk* or outcome* or clinical* or hospitalis* or hospitaliz* or deteriorat* or severity* or severe* or progress* or decision* or mortality* or death* or morbidity*)).ti,ab. 625899
30 ((outcome* or clinical* or decision* or determin*) adj3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model*)).ti,ab. 934797
31 (risk* adj3 (detect* or identif* or manag* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify* or hospitalis* or hospitaliz* or deteriorat* or severity* or severe* or progress* or mortality* or death* or morbidity*)).ti,ab. 732353
32 ((severe* or severity*) adj3 (detect* or identif* or define* or defining* or definition* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify*)).ti,ab. 169580
33 (symptom* adj3 (coalition* or cluster* or group* or collection* or assess* or criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or technique* or scale* or algorithm* or metric* or measure* or rating* or framework* or grade* or model* or stratification* or stratify*)).ti,ab. 163123
34 (statistical* adj3 (criteria* or criterion* or rule* or ruling* or score* or scoring* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or algorithm* or rating* or framework* or model*)).ti,ab. 70897
35 ((score* or scoring*) adj3 (system* or criteria* or criterion* or rule* or ruling* or tool* or index* or indice* or instrument* or checklist* or survey* or questionnaire* or appraisal* or indicator* or algorithm* or rating* or framework* or model*)).ti,ab. 173568
36 ((disease* or illness* or clinical* or identif* or detect* or alert*) adj3 (deteriorat* or progress* or exacerbat*)).ti,ab. 283287
37 or/21-36 3656227
38 20 and 37 233320
39 primary health care/ 95769
40 exp general practice/ 79821
41 physicians, primary care/ 4606
42 general practitioners/ 11509
43 Practice Patterns, Physicians'/ 68620
44 (primary* adj2 (care* or healthcare*)).ti,ab. 191838
45 ((general* or family*) adj2 (practice* or practitioner* or physician* or doctor* or medicine*)).ti,ab. 156494
46 GP.ti,ab. 51989
47 ambulatory care/ 47148

Searches – Part 2B	
48	ambulatory care facilities/ 23111
49	community health services/ 33520
50	Community Health Workers/ 6963
51	exp Community Health Nursing/ 20375
52	home care services/ or Home Health Nursing/ or Home Nursing/ 45134
53	House calls/ 4283
54	Outpatient Clinics, Hospital/ 15859
55	((ambulatory* or outpatient*) adj3 (care* or healthcare* or facility* or facilities* or clinic or clinics or department* or service* or setting*)).ti,ab. 121278
56	((community* or communities* or neighbourhood* or neighborhood*) adj2 (health* or care*) adj2 (practice* or practitioner* or physician* or doctor* or medicine* or nurs* or worker* or professional* or facility* or facilities* or clinic or clinics or auxiliar*)).ti,ab. 15185
57	((home* or house*) adj1 (call* or visit* or care* or healthcare* or nurs*)).ti,ab. 77842
58	or/39-57 757698
59	38 and 58 13189
60	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/ 2543398
61	(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. 2720288
62	Adolescent/ or Adolescent Behavior/ or Adolescent Health/ or Puberty/ 2280350
63	("under 18*" or "under eighteen*").ti,ab. 4779
64	(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. 634179
65	(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. 360815
66	or/60-65 5130397
67	59 and 66 4098
68	exp Cohort studies/ 2653429
69	((follow up* or followup* or concurrent* or incidence* or population*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. 515084
70	(longitudinal* or prospective* or retrospective* or cohort*).ti,ab. 2799368
71	epidemiologic methods/ and (197* or 198*).yr. 10282
72	Cross-Sectional Studies/ 515802
73	((prevalence* or disease frequenc*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. 69059
74	(crosssection* or crossection* or "cross section*").ti,ab. 632336
75	Validation Study/ 112475
76	Predictive Value of Tests/ 228369
77	ROC curve/ 75029
78	Prognosis/ 621229
79	((valid* or concordance* or calibrat*) adj3 (external* or study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. 244952

Searches – Part 2B
80 (prognostic* adj3 (study* or studies* or analy* or observation* or design* or method* or research* or variable*)).ti,ab. 41369
81 (c-statistic* or "area under the curve" or AUC or "Receiver operating characteristic*" or ROC).ti,ab. 291496
82 or/68-81 5470677
83 67 and 82 2347
84 Animals/ not (Animals/ and Humans/) 5226930
85 83 not 84 2347
86 limit 85 to english language 2242
87 limit 86 to (letter or historical article or comment or editorial or news or case reports) 25
88 86 not 87 2217

Additional search techniques

Forward citation searching and reference list checking (Parts 2A and 2B)

Date of search	19/9/24
How the searches were managed	Forward citation searching and reference list checking were done separately as two different operations using the same sources, seed references and decision-making criteria, and so they are reported in a single table here. These techniques covered Parts 2A and 2B at the same time, as the seed references overlapped.
How the seed papers were identified	Identified from the scoping searches and the systematic review search for Part 1.
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 2024-09-16
How results were managed	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	Did not make any decisions based on the location of the study. Did not include any papers that were about aetiology or epidemiology

	Did not include systematic reviews, guidelines, animal studies, letters or editorials Only included papers written in English.
List of seed papers used	Dean P & Florin TA (2018) Factors associated with pneumonia severity in children: a systematic review. *Journal of the Pediatric Infectious Diseases Society*, 7(4), 323-334. Deardorff KV et al. (2018) Pneumonia risk stratification scores for children in low-resource settings: a systematic literature review. *Pediatric Infectious Disease Journal*, 37(8), 743-748. Edwards G et al. (2021) Predicting poor outcomes in children aged 1-12 with respiratory tract infections: a systematic review. *PLoS ONE*, 16(4), e0249533. Hay AD et al. (2016) Development and internal validation of a clinical rule to improve antibiotic use in children presenting to primary care with acute respiratory tract infection and cough: a prognostic cohort study. *Lancet Respiratory Medicine*, 4(11), 902-910. Nijman RG et al. (2013) Clinical prediction model to aid emergency doctors managing febrile children at risk of serious bacterial infections: diagnostic study. *BMJ*, 346, f1706. Wildes DM et al. (2021) A systematic review of clinical prediction rules to predict hospitalisation in children with lower respiratory infection in primary care and their validation in a new cohort. *EClinicalMedicine*, 41, 101164. Williams DJ et al. (2016) Predicting severe pneumonia outcomes in children. *Pediatrics*, 138(4).
No. of forward citation searching results	254
No. of reference list checking results	219

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 October 11, 2024	157

Search strategy history

Database name: Econlit

Searches	
1	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).af. 150

Searches
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
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

Searches
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
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
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

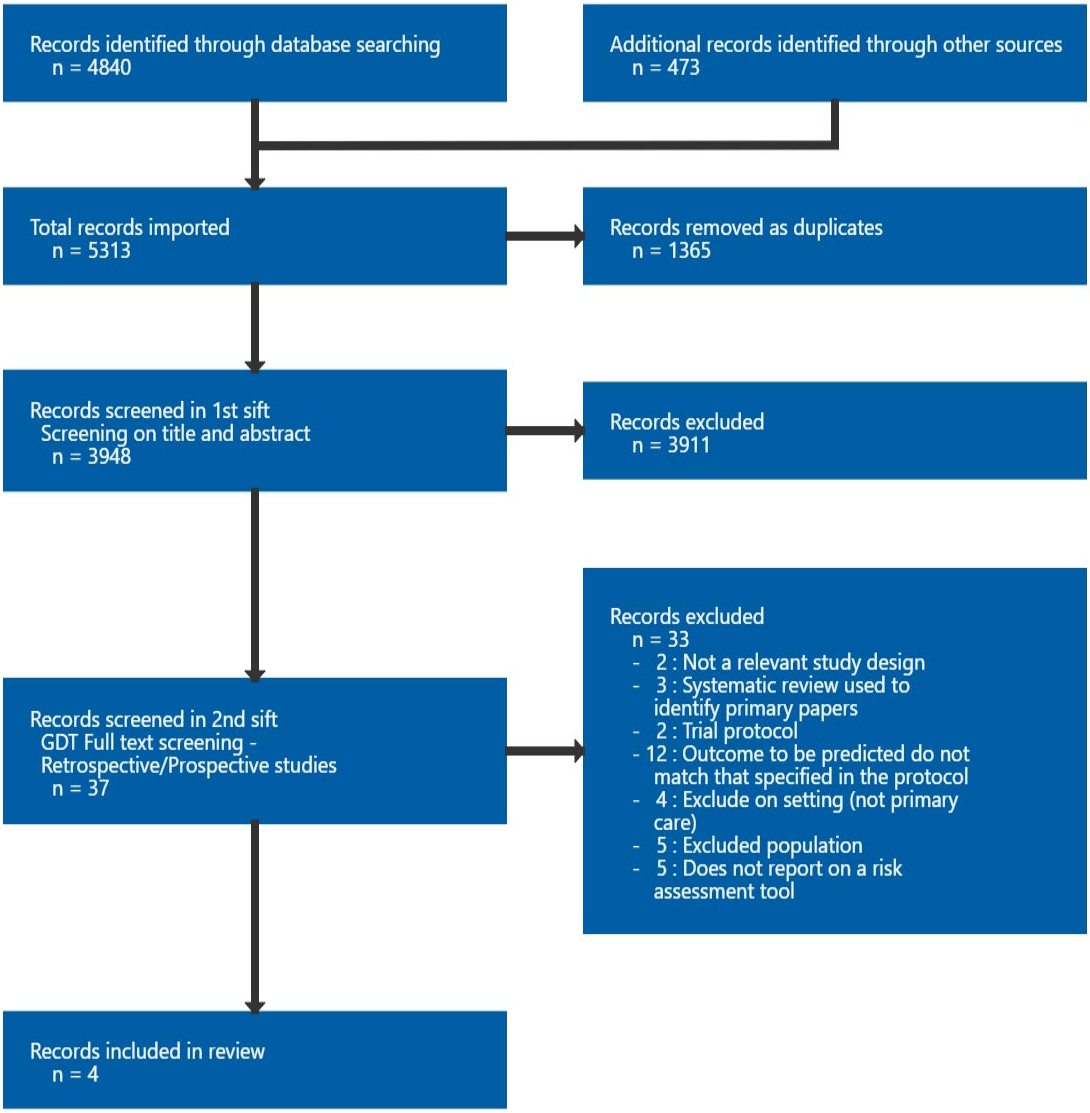
Searches
22 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 3930
23 (european* adj2 quality adj3 ("5" or five)).tw. 723
24 or/4-23 506237
25 3 and 24 3855
26 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa 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
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

Searches	
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 – Prognostic evidence study selection



Appendix D – Prognostic evidence

Bos, 2023

Bibliographic Reference	Bos, David A G; De Burghgraeve, Tine; De Sutter, An; Buntinx, Frank; Verbakel, Jan Y; Clinical prediction models for serious infections in children: external validation in ambulatory care.; BMC medicine; 2023; vol. 21 (no. 1); 151

Study Characteristics

Study design	Prospective cohort study
Study details	Study location: Belgium Study setting: Primary care: general practices (n=92), outpatient paediatric practices (n=6) or emergency departments (n=6) Study dates: 15th Feb 2013 to 28th Feb 2014 Sources of funding: This study was funded by the National Institute for Health and Disability Insurance (RIZIV, Belgium) under reference CGV n° 2012/235 and the Research Foundation Flanders (FWO Vlaanderen) under research project n° G067509N.
Inclusion criteria	Children aged 1 month to 16 years presenting to a family physician or paediatrician with a new acute illness episode of maximum 5 days.
Exclusion criteria	Children were excluded if the acute illness was caused by purely traumatic or neurological conditions, intoxication, a psychiatric problem or an exacerbation of a known chronic condition.
Number of participants and recruitment methods	A total of 8962 acutely ill children were initially included, but 730 were subsequently excluded due to missing essential data (age, sex, temperature, outcome) and 21 for exceeding the age range, leading to 8211 participants in the final analysis. Eligible children were recruited consecutively during the inclusion period by participating physicians. If a physician included less than 5 children over the study period, the assumption of consecutive inclusion was considered violated so their results were subsequently excluded from the analysis.
Length of follow-up	N/A
Loss to follow up	N/A

Outcome(s) of interest	Serious infection requiring hospital admission for more than 24 hours (including sepsis and bacteraemia, meningitis, pneumonia (radiological criteria required for definitive diagnosis), osteomyelitis, cellulitis and cUTI as well as appendicitis, gastro-enteritis with dehydration and viral respiratory tract infection with hypoxia).
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	4 clinical prediction models: 1. Feverkidstool 2. Craig model 3. SBI score (not extracted; no data for pneumonia patients) 4. Paediatric Advanced Warning Score (PAWS) (not extracted; no data for pneumonia patients)
Covariates adjusted for in the multivariable regression modelling	None reported
Additional comments	Although the sample was recruited in mainly primary care settings (GP n = 2902; ambulatory paediatrician n = 2719; ED n = 2590), the large majority of SIs were diagnosed in patients seen in the ED: GP n = 23, ambulatory paediatrician n = 109; ED n = 366. Separate analyses by setting were not reported. The clinical prediction models tested were largely developed and internally validated in ED settings. This study aimed to externally validate them in primary care settings, but the prevalence of serious infections can differ between GP and ED settings.

Notes: cUTI: complicated urinary tract infection; SBI: Serious bacterial infection; ED: emergency department

Population characteristics

Arm-level characteristics

Characteristic	Children with serious infection (N = 498)	Children without serious infection (N = 7713)
% Female No of events	n = 230 ; % = 46.2	n = 3580 ; % = 46.4
Median age (IQR) (years)	1.62 (0.78 to 3.79)	1.97 (0.99 to 4.02)

Characteristic	Children with serious infection (N = 498)	Children without serious infection (N = 7713)
Inclusion setting - Inclusion by GP (n=2902) No of events	n = 23 ; % = 0.8	n = 2879 ; % = 99.2
Inclusion setting - Inclusion by ambulatory paediatrician (n=2719) No of events	n = 109 ; % = 4	n = 2610 ; % = 96
Inclusion setting - Inclusion by ED (n=2590) No of events	n = 366 ; % = 14.1	n = 2224 ; % = 85.9

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Partially indirect *(Overall sample is patients with any serious infection; subgroup analyses presented for pneumonia but rates of pneumonia in this sample are very low (2%))*

Gallagher, 2021

Bibliographic Reference	Gallagher, Joe; Chisale, Master; Das, Sudipto; Drew, Richard J; Glezeva, Nadezhda; Wildes, Dermot Michael; De Gascun, Cillian; Wu, Tsung-Shu Joseph; Ledwidge, Mark T; Watson, Chris; Aetiology and severity of childhood pneumonia in primary care in Malawi: a cohort study.; BMJ open; 2021; vol. 11 (no. 7); e046633

Study Characteristics

Study design	Prospective cohort study
Study details	Study location: Malawi Study setting: A community health centre and the outpatient department of a central hospital in Northern Malawi, both of which serve as primary care facilities for this urban area. 98%

	of participants were recruited from the community health centre. Study dates: March to June 2016 Sources of funding: This work was conducted with the generous support of the Bill & Melinda Gates Foundation – Investment ID: OPP1139557.
Inclusion criteria	Children aged 2-59 months presenting to primary care with a main complaint of cough or difficulty breathing associated with tachypnoea (defined as >50 breaths per minute if aged 2–11 months or >40 breaths per minute age if aged 12–59 months) or chest in-drawing. This is the current WHO clinical case definition of pneumonia.
Exclusion criteria	Those discharged from hospital in the preceding 30 days; those who had completed a course of antibiotics within 14 days of presentation; or those who had received antibiotics prior to clinical assessment for this illness.
Number of participants and recruitment methods	Of 615 children approached for participation, 494 (80.3%) were included in the final sample; 121 were excluded because they either did not meet inclusion criteria (n=65), refused (n=26), or withdrew (n=30). All children presenting to primary care during the study period were assessed for study eligibility and enrolment.
Length of follow-up	Children were followed up by telephone by contacting their caregiver at 7 days and 30 days following their initial assessment.
Loss to follow up	Of the initial sample (n=494), 225 caregivers were contactable on day 7 and all children were alive, and 195 were contactable on day 30 and 2 children had died.
Outcome(s) of interest	Hospitalisation (within 30 days)
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	Individual signs and symptoms: Difficulty breathing; deep breathing; respiratory rate; age; wheeze; lower chest wall indrawing. 'Difficulty drawing breath' model: assigned a score of 1 to each sign or symptom present (categorical treatment of age <2 years and respiratory rate >70bpm) and generated a simple 7-point score for each patient.
Covariates adjusted for in the multivariable regression modelling	Malaria status, HIV status, number of vaccinations, number of people usually sleeping in the same room as the child, presence of chimney for indoor fire, availability of electricity in the home, and distance from the nearest health clinic.

Additional comments	Study was conducted in an area of high immunisation uptake and where the prevalence of bacterial pneumonia in children presenting to primary care is low.

Notes: WHO: World Health Organisation

Population characteristics

Study-level characteristics

Characteristic	Study (N = 494)
% Female No of events	n = 223 ; % = 43.2
Median age (IQR) (months)	18 (10 to 30)
Age (months) - 2-11 months No of events	n = 157 ; % = 31.8
Age (months) - 12-35 months No of events	n = 252 ; % = 51
Age (months) - 36-60 months No of events	n = 85 ; % = 17.2

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate *(Method of outcome assessment unclear - appears to rely on self-report by caregivers via phone calls at 7- and 30-days. Hospital records not obtained to confirm admission.)*
Overall Risk of bias and Applicability	Concerns for applicability	Partially indirect *(Study was conducted in Malawi where the health care system may differ from the UK.)*

Hay, 2016

Bibliographic Reference	Hay, Alastair D; Redmond, Niamh M; Turnbull, Sophie; Christensen, Hannah; Thornton, Hannah; Little, Paul; Thompson, Matthew; Delaney, Brendan; Lovering, Andrew M; Muir, Peter; Leeming, John P; Vipond, Barry; Stuart, Beth; Peters, Tim J; Blair, Peter S; Development and internal validation of a clinical rule to improve antibiotic use in children presenting to primary care with acute respiratory tract infection and cough: a prognostic cohort

study.; The Lancet. Respiratory medicine; 2016; vol. 4 (no. 11); 902-910

Study Characteristics

Study design	Prospective cohort study
Study details	Study location: UK Study setting: 247 primary care practices Study dates: July 2011 to June 2013 Sources of funding: This paper presents independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (Grant Reference Number RP-PG-0608-10018) and led by researchers at the University of Bristol and NHS Bristol Clinical Commissioning Group. ADH is funded by NIHR Research Professorship (NIHR-RP-02-12-012) and HC by an NIHR post-doctoral fellowship (PDF-2012-05-245).
Inclusion criteria	Children aged between 3 months and 16 years, presenting to primary care with the main symptom of acute (≤28 days) cough with other respiratory tract infection symptoms (such as fever and coryza). Children with an infected exacerbation of asthma and those who were severely unwell (eg, requiring same day hospital assessment or admission) were included.
Exclusion criteria	Children were excluded if they presented with a noninfective exacerbation of asthma, were at high risk of serious infection (immunocompromised, for example with cystic fibrosis), required a throat swab for clinical management (which were taken for research purposes in a subgroup of children), had been previously recruited to the study or recently participated in other research, or had temporarily registered at the practice.
Number of participants and recruitment methods	Clinicians offered 9043 invitations to children for study recruitment, of which 8879 (98%) were accepted, and for which 8394 (95%) received the children's parents' valid consent; all these children met the eligibility criteria and made up the final analytical sample.
Length of follow-up	30 days after initial consultation
Loss to follow up	N/A
Outcome(s) of interest	Hospital admission for any respiratory tract infection in the 30 days after recruitment (excluding emergency department attendance only)

Prognostic factors or risk factor(s) or sign(s)/symptom(s)	Clinicians completed a structured online (or paper) case report form, which recorded eight sociodemographic and four past medical history items, 33 parent-reported symptoms (including symptom severity of either mild, moderate, or severe in the previous 24 h), 14 physical examination signs (including vital signs and global illness severity), and the prescription of antibiotics. Children were assessed for current asthma at medical notes review. The final multivariable model generated a simple one-point-per-item rule consisting of: short (≤3 days) illness; temperature; age (<24 months); recession; wheeze; asthma; and vomiting.
Covariates adjusted for in the multivariable regression modelling	Not reported
Additional comments	78/8394 children (0·9%, 95% CI 0·7%–1·2%) were admitted to hospital for a respiratory tract infection in the 30 days after recruitment. Median time to hospital admission was 2 days (IQR 1–11), with 15 (19%) of children admitted to hospital on the day of recruitment (day 1), 33 (42%) admitted between days 2 and 7, 11 (14%) admitted between days 8 and 14, and 19 (24%) admitted between days 15 and 30. This means that the STARWAVe score only provides a risk of admission within 30 days; not whether a child presenting to their GP needs to be referred for immediate secondary care review. Hospital discharge diagnoses were lower respiratory tract infection (15 [19%]); bronchiolitis (14 [18%]); viral wheeze (12 [15%]); upper respiratory tract infection (ten [13%]); croup (six [8%]); infected exacerbation of asthma (six [8%]); tonsillitis (five [6%]); viral illness (four [5%]); febrile illness (two [3%]); pneumonia (one [1%]) and missing data (three [4%]), so the STARWAVe tool is not specific to pneumonia.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 8394)
% Female No of events	n = 4029 ; % = 48
Median age (IQR) (years)	3 (1 to 6)

Characteristic	Study (N = 8394)
Number of children hospitalised	N = 78, % = 0.9
Hospital discharge diagnoses - LRTI No of events, % of those hospitalised	n = 15 ; % = 19
Hospital discharge diagnoses - Bronchiolitis No of events, % of those hospitalised	n = 14 ; % = 18
Hospital discharge diagnoses - Viral wheeze No of events, % of those hospitalised	n = 12 ; % = 15
Hospital discharge diagnoses - URTI No of events, % of those hospitalised	n = 10 ; % = 13
Hospital discharge diagnoses - Croup No of events, % of those hospitalised	n = 6 ; % = 8
Hospital discharge diagnoses - Infected exacerbation of asthma No of events, % of those hospitalised	n = 6 ; % = 8
Hospital discharge diagnoses - Tonsillitis No of events, % of those hospitalised	n = 5 ; % = 6
Hospital discharge diagnoses - Viral illness No of events, % of those hospitalised	n = 4 ; % = 5
Hospital discharge diagnoses - Febrile illness No of events, % of those hospitalised	n = 2 ; % = 3
Hospital discharge diagnoses - Pneumonia No of events, % of those hospitalised	n = 1 ; % = 1

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low

Section	Question	Answer
Overall Risk of bias and Applicability	Concerns for applicability	Partially indirect *(Participants were those with any LRTI symptoms and not specifically those with suspected pneumonia. Final diagnostic information showed a very low prevalence of pneumonia in this sample (1%))*

Wildes, 2021

Bibliographic Reference	Wildes, Dermot M; Chisale, Master; Drew, Richard J; Harrington, Peter; Watson, Chris J; Ledwidge, Mark T; Gallagher, Joe; A Systematic Review of Clinical Prediction Rules to Predict Hospitalisation in Children with Lower Respiratory Infection in Primary Care and their Validation in a New Cohort.; EClinicalMedicine; 2021; vol. 41; 101164

Study Characteristics

Study design	Prospective cohort study
Study details	Study location: Malawi Study setting: 2 primary care facilities Study dates: March to June 2016 Sources of funding: This study was funded in whole or in part by the support of the Bill & Melinda Gates Foundation (Investment ID: OPP1139557). The foundation was not involved in study design, data collection, analysis, interpretation or drafting of this report.
Inclusion criteria	Children aged 2-59 months with WHO clinically defined pneumonia presenting to primary care.
Exclusion criteria	Those discharged from hospital in the preceding 30 days; those who had completed a course of antibiotics within 14 days of presentation; or those who had received antibiotics prior to clinical assessment for this illness. *(Information taken from Gallagher 2021; primary publication)*
Number of participants and recruitment methods	All children presenting to primary care during the study period were assessed for study eligibility and enrolment. Of 615 children approached for participation, 494 (80.3%) were included in the final sample; 121 were excluded because they either did not meet inclusion criteria (n=65), refused (n=26), or withdrew (n=30). *(Information taken from Gallagher 2021; primary publication)*

Length of follow-up	Children were followed up by telephone by contacting their caregiver at 7 days and 30 days following their initial assessment. *(Information taken from Gallagher 2021; primary publication)*
Loss to follow up	Of the initial sample (n=494), 225 caregivers were contactable on day 7 and all children were alive, and 195 were contactable on day 30 and 2 children had died. *(Information taken from Gallagher 2021; primary publication)*
Outcome(s) of interest	Hospitalisation (within 30 days)
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	STARWAVe clinical prediction rule: current asthma; age (<2 years); inter-/sub-costal recession; illness duration (<4 days); moderate to severe vomiting (within 24 hours of presenting); wheeze; and body temperature (>37.8 degrees celcius or parent-reported severe fever within 24 hours of presenting) were the predictors employed by the final model.
Covariates adjusted for in the multivariable regression modelling	N/A
Additional comments	There was no child with a diagnosis of asthma in the external validation cohort. This may be due to under-diagnosis, and may have impacted the results of the model performance. In the STARWAVe study, 750 of the children included in the study have a concomitant diagnosis of asthma, comprising almost 10% of the sample population. Asthma was one of the predictor parameters associated with hospital admission, so the potential under-diagnosis of asthma in the validation sample may have impacted model performance.

Notes: WHO: World Health Organisation

Population characteristics

Study-level characteristics

Characteristic	Study (N = 494)
% Female No of events	n = 223 ; % = 43.2
Median age (IQR) (months)	18 (10 to 30)

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate *(Method of outcome assessment unclear - appears to rely on self-report by caregivers via phone calls at 7- and 30-days. Hospital records not obtained to confirm admission.)*
Overall Risk of bias and Applicability	Concerns for applicability	Indirect *(Study was conducted in Malawi where the health care system may differ from the UK. No participants in this sample had a diagnosis of asthma (one of the STARWAVe criteria), which may have impacted the performance of the model; likely due to under-diagnosis of asthma in this region.)*

Appendix E – Forest plots

No forest plots required for this review.

Appendix F – GRADE tables

F.1 C-statistics

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Feverkidstool (updated model); pneumonia requiring hospital admission								
Bos 2023	Prospective cohort	8049	0.83 (0.80 to 0.86)	No serious	Serious[1]	Serious[2]	No serious	Low
Craig model (updated model); pneumonia requiring hospital admission								
Bos 2023	Prospective cohort	8049	0.83 (0.80 to 0.86)	No serious	Serious[1]	Serious[2]	No serious	Low

[1] Downgraded once because study was assessed as partially indirect

[2] Downgraded once for inconsistency – single study

F.2 Area under the curve (AUC)

No. of studies	Study design	Sample size	AUC (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
'Difficulty drawing breath' model; hospital admission								
Gallagher 2021	Prospective cohort	494	0.91 (0.87 to 0.95)	Serious[1]	Serious[2]	Serious[3]	No serious	Very low
STARWAVe; hospital admission within 30 days								
Hay 2016	Prospective cohort	8394	0.81 (0.76 to 0.85)	No serious	Serious[2]	Serious[3]	Serious[4]	Very low
STARWAVe; hospital admission within 30 days								

No. of studies	Study design	Sample size	AUC (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Wildes 2021	Prospective cohort	494	0.80 (0.75 to 0.85)	Serious[1]	Very serious[5]	Serious[3]	Serious[4]	Very low

[1] Downgraded once for moderate concerns about risk of bias
[2] Downgraded once because study was assessed as partially indirect
[3] Downgraded once for inconsistency: single study
[4] Downgraded once because 95%CI crosses 1 decision making threshold (test classification accuracy thresholds)
[5] Downgraded twice because study was assessed as indirect

F.3 Calibration statistics

F.3.1 Calibration slope

No. of studies	Study design	Sample size	Calibration slope (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Feverkidstool (updated model); pneumonia vs absence of SBI								
Bos 2023	Prospective cohort	8049	1.04 (0.92 to 1.17)	Not serious	Serious[1]	Serious[2]	N/A[3]	Low
Craig model (updated model); pneumonia vs absence of SBI								
Bos 2023	Prospective cohort	8049	1.05 (0.93 to 1.18)	Not serious	Serious[1]	Serious[2]	N/A[3]	Low

[1] Downgraded once because study was assessed as partially indirect
[2] Downgraded once for inconsistency: single study
[3] Not possible to assess imprecision

F.3.2 Calibration intercept

No. of studies	Study design	Sample size	Calibration intercept (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Feverkidstool (updated model); pneumonia vs absence of SBI								
Bos 2023	Prospective cohort	8049	0.00 (-0.16 to 0.16)	Not serious	Serious[1]	Serious[2]	N/A[3]	Low
Craig model (updated model); pneumonia vs absence of SBI								
Bos 2023	Prospective cohort	8049	0.00 (-0.16 to 0.16)	Not serious	Serious[1]	Serious[2]	N/A[3]	Low

[1] Downgraded once because study was assessed as partially indirect
[2] Downgraded once for inconsistency: single study
[3] Not possible to assess imprecision

F.4 Prognostic accuracy measures for risk of hospitalisation

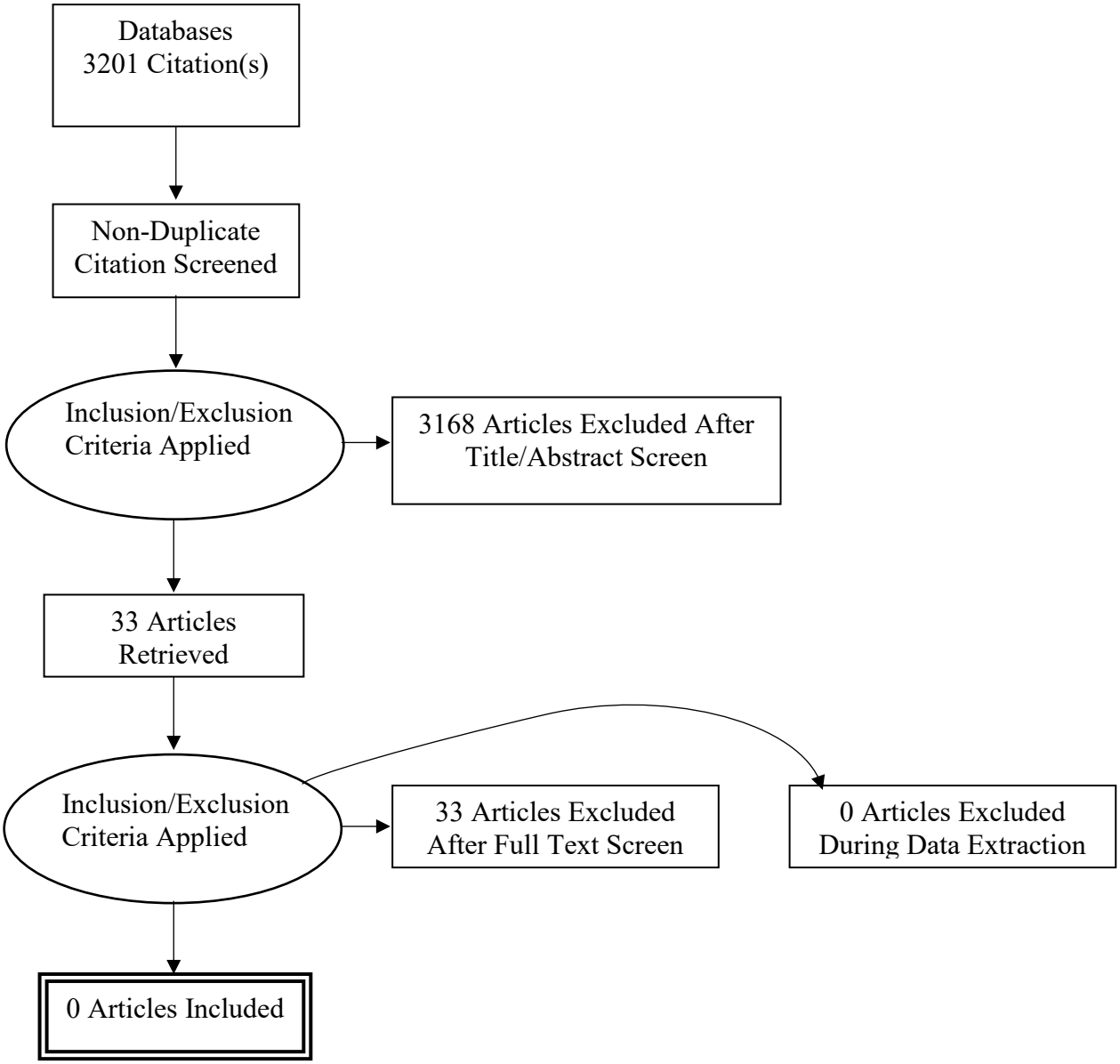
No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Feverkidstool (updated in Bos 2023): Risk ≥2.5% (low risk cut-off). Outcome: pneumonia requiring hospital admission										
Bos 2023	Prospective cohort	8049	0.71 (0.64 to 0.78)	0.77 (0.76 to 0.78)	LR+ 3.09 (2.79 to 3.42)	Not serious	Serious[1]	Serious[2]	Not serious	Low
					LR- 0.37 (0.29 to 0.47)	Not serious	Serious[1]	Serious[2]	Not serious	Low
Feverkidstool (updated in Bos 2023): Risk ≥10% (high risk cut-off). Outcome: pneumonia requiring hospital admission										

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Bos 2023	Prospective cohort	8049	0.29 (0.22 to 0.36)	0.98 (0.97 to 0.98)	LR+ 12.40 (9.41 to 16.36)	Not serious	Serious[1]	Serious[2]	Not serious	Low
					LR- 0.73 (0.66 to 0.80)	Not serious	Serious[1]	Serious[2]	Not serious	Low
Feverkidstool (updated in Bos 2023): Risk ≥30% (high risk cut-off). Outcome: pneumonia requiring hospital admission										
Bos 2023	Prospective cohort	8049	0.08 (0.04 to 0.13)	1.00 (1.00 to 1.00)	LR+ 31.52 (15.83 to 62.78)	Not serious	Serious[1]	Serious[2]	Not serious	Low
					LR- 0.93 (0.89 to 0.97)	Not serious	Serious[1]	Serious[2]	Not serious	Low
Craig model (updated in Bos 2023): Risk ≥2.5% (low risk cut-off). Outcome: pneumonia requiring hospital admission										
Bos 2023	Prospective cohort	8211	0.69 (0.61 to 0.76)	0.81 (0.80 to 0.81)	LR+ 3.56 (3.19 to 3.97)	Not serious	Serious[1]	Serious[2]	Not serious	Low
					LR- 0.38 (0.31 to 0.48)	Not serious	Serious[1]	Serious[2]	Not serious	Low
Craig model (updated in Bos 2023): Risk ≥10% (high risk cut-off). Outcome: pneumonia requiring hospital admission										
Bos 2023	Prospective cohort	8211	0.27 (0.21 to 0.35)	0.97 (0.97 to 0.98)	LR+ 10.89 (8.24 to 14.39)	Not serious	Serious[1]	Serious[2]	Not serious	Low
					LR- 0.74 (0.68 to 0.82)	Not serious	Serious[1]	Serious[2]	Not serious	Low
Craig model (updated in Bos 2023): Risk ≥30% (high risk cut-off). Outcome: pneumonia requiring hospital admission										
Bos 2023	Prospective cohort	8211	0.08 (0.04 to 0.13)	1.00 (1.00 to 1.00)	LR+ 43.66 (20.84 to 91.47)	Not serious	Serious[1]	Serious[2]	Not serious	Low
					LR- 0.93 (0.89 to 0.97)	Not serious	Serious[1]	Serious[2]	Not serious	Low

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
'Difficulty drawing breath' model (Gallagher 2021): Score ≥3 (intermediate- to high-risk). Outcome: hospitalisation										
Gallagher 2021	Prospective cohort	494	0.88 (0.86 to 0.95)	0.84 (0.80 to 0.87)	LR+ Not reported	N/A	N/A	N/A	N/A	N/A
					LR- Not reported	N/A	N/A	N/A	N/A	N/A
STARWAVe (Hay 2016): Normal or high risk vs very low risk. Outcome: hospitalisation within 30 days										
Hay 2016	Prospective cohort	8394	0.78 (not reported)	0.68 (not reported)	LR+ Not reported	N/A	N/A	N/A	N/A	N/A
					LR- Not reported	N/A	N/A	N/A	N/A	N/A
STARWAVe (Hay 2016): High risk vs normal or very low risk. Outcome: hospitalisation within 30 days										
Hay 2016	Prospective cohort	8394	0.31 (not reported)	0.98 (not reported)	LR+ Not reported	N/A	N/A	N/A	N/A	N/A
					LR- Not reported	N/A	N/A	N/A	N/A	N/A
STARWAVe (Wildes 2021): Score ≥4 (high risk)										
Wildes 2021	Prospective cohort	494	0.32 (0.20 to 0.46)	0.91 (0.88 to 0.94)	LR+ Not reported	N/A	N/A	N/A	N/A	N/A
					LR- Not reported	N/A	N/A	N/A	N/A	N/A

[1] Downgraded once because study assessed as partially indirect
[2] Downgraded once for inconsistency: single study
Note: GRADE applied to LRs (not sensitivity and specificity) and where LRs were not reported, GRADE was not applied (N/A).

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

No studies were included in this review question.

Appendix I – Health economic model

No original health economic modelling was done for this review question.

Appendix J – Excluded studies

Prognostic studies

Study	Reason
Anteneh, ZA Arega, HE Mihretie, KM (2023) Validation of risk prediction for outcomes of severe community-acquired pneumonia among under-five children in Amhara region, Northwest Ethiopia. PLOS ONE 18(2)	- Exclude on setting (not primary care) *Participants were children hospitalised with severe CAP; risk assessment tool was designed for use in hospitals to predict treatment failure or death.*
Bhat, JI Charoo, BA Mukherjee, A Ahad, R Das, RR Goyal, JP Vyas, B Ratageri, VH Lodha, R (2021) Risk of Hospitalization in Under-five Children With Community-Acquired Pneumonia: A Multicentric Prospective Cohort Study. INDIAN PEDIATRICS 58(11): 1019 - 1023	- Does not report on a risk assessment tool *Reports multivariate analysis of factors associated with risk of hospitalisation, but does not present them as a tool or scoring system for risk assessment*
Blacklock, C. Mayon-White, R. Coad, N. Thompson, M. (2011) Which symptoms and clinical features correctly identify serious respiratory infection in children attending a paediatric assessment unit?. ARCHIVES OF DISEASE IN CHILDHOOD 96(8): 708 - 714	- Does not report on a risk assessment tool *Reports on individual symptoms that are predictive of a diagnosis of pneumonia. Does not provide an assessment tool and does not predict need for hospitalisation.*
Blair, PS Young, G Clement, C Dixon, P Seume, P Ingram, J Taylor, J Cabral, C Lucas, PJ Beech, E Horwood, J Gulliford, M Francis, NA Creavin, S Lane, JA Bevan, S D Hay, A (2023) Multi-faceted intervention to improve management of antibiotics for children presenting to primary care with acute cough and respiratory tract infection (CHICO): efficient cluster randomised controlled trial. BMJ-BRITISH MEDICAL JOURNAL 381	- Not a relevant study design *RCT comparing Starwave plus other intervention materials (antibiotic prescribing guidance, safety net leaflet for parents/carers) vs usual care; primary outcome antibiotic prescribing and hospitalisation. No data on performance of starwave or use to make decisions about hospitalisation*
Blair, PS Young, GJ Clement, C Dixon, P Seume, P Ingram, J Taylor, J Horwood, J Lucas, PJ Cabral, C Francis, NA Beech, E Gulliford, M Creavin, S Lane, JA Bevan, S Hay, AD (2023) A multifaceted intervention to reduce antibiotic prescribing among CHIldren with acute COugh and respiratory tract infection: the CHICO cluster RCT. HEALTH TECHNOLOGY ASSESSMENT 27(32)	- Not a relevant study design *RCT comparing Starwave plus other intervention materials (antibiotic prescribing guidance, safety net leaflet for parents/carers) vs usual care; primary outcome antibiotic prescribing and hospitalisation. No data on performance of starwave or use to make decisions about hospitalisation*
Chandna, A., Lubell, Y., Mwandigha, L. et al. (2022) Defining the role of host	- Outcome to be predicted do not match that specified in the protocol

Study	Reason
biomarkers in the diagnosis and prognosis of childhood pneumonia - a prospective cohort study. medRxiv	*Use of LqSOFA tool to predict need for supplemental oxygen - did not report on need for hospitalisation*
Chandna, A., Mwandigha, L., Koshiaris, C. et al. (2022) External validation and updating of clinical severity scores to guide referral of young children with acute respiratory infections in resource-limited primary care settings. medRxiv	- Outcome to be predicted do not match that specified in the protocol *Use of LqSOFA tool to predict primary outcome of need for supplemental oxygen - did not report on need for hospitalisation*
Chandna, Arjun, Mwandigha, Lazaro, Koshiaris, Constantinos et al. (2023) External validation of clinical severity scores to guide referral of paediatric acute respiratory infections in resource-limited primary care settings. Scientific reports 13(1): 19026	- Outcome to be predicted do not match that specified in the protocol *Use of LqSOFA tool to predict need for supplemental oxygen - did not report on need for hospitalisation*
Deardorff, Katrina V. McCollum, Eric D. Ginsburg, Amy Sarah (2018) Pneumonia Risk Stratification Scores for Children in Low-Resource Settings: A Systematic Literature Review. PEDIATRIC INFECTIOUS DISEASE JOURNAL 37(8): 743 - 748	- Outcome to be predicted do not match that specified in the protocol *Reviewed risk assessment scores for predicting mortality or treatment failure.*
Edwards, George, Newbould, Louise, Nesbitt, Charlotte et al. (2021) Predicting poor outcomes in children aged 1-12 with respiratory tract infections: A systematic review. PloS one 16(4): e0249533	- Systematic review used to identify primary papers
Florin, TA Ambroggio, L Lorenz, D Kachelmeyer, A Ruddy, RM Kuppermann, N Shah, SS (2021) Development and Internal Validation of a Prediction Model to Risk Stratify Children With Suspected Community-Acquired Pneumonia. CLINICAL INFECTIOUS DISEASES 73(9): E2713 - E2721	- Exclude on setting (not primary care) *Tool for use in emergency departments not primary care. Also this was a development and internal validation study; tool has not been externally validated. Outcome was disease severity not need for hospitalisation*
Hay, Alastair D, Fahey, Tom, Peters, Tim J et al. (2004) Predicting complications from acute cough in pre-school children in primary care: a prospective cohort study. The British journal of general practice : the journal of the Royal College of General Practitioners 54(498): 9-14	- Outcome to be predicted do not match that specified in the protocol *Looks at symptoms most predictive of complications in children with acute cough. Outcome is presence of complications and not specific to hospital admission. Population is children with acute cough; not specific to pneumonia. Internal validation study; no external validation reported.*
Hay, Alastair D, Gorst, Catharine, Montgomery, Alan et al. (2007) Validation of	- Outcome to be predicted do not match that specified in the protocol

Study	Reason
a clinical rule to predict complications of acute cough in preschool children: a prospective study in primary care. The British journal of general practice : the journal of the Royal College of General Practitioners 57(540): 530-7	*Validation study for CPR previously excluded. Looks at symptoms most predictive of complications in children with acute cough. Outcome is presence of complications and not specific to hospital admission. Population is children with acute cough; not specific to pneumonia.*
Hayward, Gail; Thompson, Matthew; Hay, Alastair D (2012) What factors influence prognosis in children with acute cough and respiratory tract infection in primary care?. BMJ (Clinical research ed.) 345: e6212	- Systematic review used to identify primary papers
Little, Paul, Becque, Taeko, Hay, Alastair D et al. (2023) Predicting illness progression for children with lower respiratory infections in primary care: a prospective cohort and observational study. The British journal of general practice : the journal of the Royal College of General Practitioners 73(737): e885-e893	- Excluded population *Although the sample had LRTI, the study states that they excluded all children where the clinician suspected pneumonia; it was restricted to uncomplicated LRTI only so not relevant to children with pneumonia.*
Mahajan, Vidushi Tiwari, Mudita Arya, Adhi Tiwari, Abhimanyu Chawla, Deepak Saini, Shiv Sajan (2016) Clinical predictors of hospital admission in acute lower respiratory tract infection in 2 months to 2-year-old children. RESPIROLOGY 21(2): 350 - 356	- Exclude on setting (not primary care) *Development of a tool for use in emergency departments. Study reports on development of the clinical risk score but no external validation. Population is children with ARI; 25% had pneumonia.*
Martin, Alexander James, van der Velden, Fabian Johannes Stanislaus, von Both, Ulrich et al. (2023) External validation of a multivariable prediction model for identification of pneumonia and other serious bacterial infections in febrile immunocompromised children. Archives of disease in childhood 109(1): 58-66	- Excluded population *Immunocompromised children*
Ramgopal, S Lorenz, D Navanandan, N Cotter, JM Shah, SS Ruddy, RM Ambroggio, L Florin, TA (2022) Validation of Prediction Models for Pneumonia Among Children in the Emergency Department. PEDIATRICS 150(1)	- Outcome to be predicted do not match that specified in the protocol *Looked a prediction models for the diagnosis of radiographic pneumonia in ED; outcome was not decision to refer to hospital*
Rebnord, IK Sandvik, H Mjelle, AB Hunskaar, S (2017) Factors predicting antibiotic prescription and referral to hospital for children with respiratory symptoms: secondary analysis of a randomised controlled study at out-of-hours services in primary care. BMJ OPEN 7(1)	- Does not report on a risk assessment tool *Not a risk assessment tool or model - presents individual symptoms predictive of hospital referral only. Small proportion of pneumonia patients.*

Study	Reason
Redmond, Niamh M, Davies, Rachel, Christensen, Hannah et al. (2013) The TARGET cohort study protocol: a prospective primary care cohort study to derive and validate a clinical prediction rule to improve the targeting of antibiotics in children with respiratory tract illnesses. BMC health services research 13: 322	- Trial protocol
Reed, Carrie Madhi, Shabir A. Klugman, Keith P. Kuwanda, Locadiah Ortiz, Justin R. Finelli, Lyn Fry, Alicia M. (2012) Development of the Respiratory Index of Severity in Children (RISC) Score among Young Children with Respiratory Infections in South Africa. PLOS ONE 7(1)	- Outcome to be predicted do not match that specified in the protocol *Tool for predicting in-hospital mortality in children hospitalised with severe LRTI*
Rees, CA Colbourn, T Hooli, S King, C Lufesi, N McCollum, ED Mwansambo, C Cutland, C Madhi, SA Nunes, M Matthew, JL Addo-Yobo, E Chisaka, N Hassan, M Hibberd, PL Jeena, PM Lozano, JM MacLeod, WB Patel, A Thea, DM Nguyen, NTV Kartasasmita, CB Lucero, M Awasthi, S Bavdekar, A Chou, M Nymadawa, P Pape, JW Paranhos-Baccala, G Picot, VS Rakoto-Andrianarivelo, M Rouzier, V Russomando, G Sylla, M Vanhems, P Wang, JW Asghar, R Banajeh, S Iqbal, I Maulen-Radovan, I Mino-Leon, G Saha, SK Santosham, M Sing (2022) Derivation and validation of a novel risk assessment tool to identify children aged 2-59 months at risk of hospitalised pneumonia-related mortality in 20 countries. BMJ GLOBAL HEALTH 7(4)	- Outcome to be predicted do not match that specified in the protocol *Tool for assessing risk of in-hospital mortality for children hospitalised with pneumonia. Not for use in primary care and does not assess need for hospitalisation.*
Shann, F; Hart, K; Thomas, D (1984) Acute lower respiratory tract infections in children: possible criteria for selection of patients for antibiotic therapy and hospital admission. Bulletin of the World Health Organization 62(5): 749-53	- Does not report on a risk assessment tool *Does not present a risk assessment tool or clinical prediction rule. Reports on rates of various symptoms in children admitted to hospital with pneumonia. Does not report on symptom rates in children not admitted.*
Thompson, M., Coad, N., Harnden, A. et al. (2009) How well do vital signs identify children with serious infections in paediatric emergency care?. Archives of Disease in Childhood 94(11): 888-893	- Exclude on setting (not primary care) *Children presenting to hospital paediatric assessment unit (51% had been referred from primary care and 16% had been brought in by ambulance); looked at signs and symptoms predictive of illness severity. Results for hospitalisation (not admitted or admitted for <1 day vs. admitted for >1 days) reported in supplementary material, but these are for all serious infections*

Study	Reason
	combined (and pneumonia only 9.6% of study population).
Thompson, M, Van den Bruel, A, Verbakel, J et al. (2012) Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care. Health technology assessment (Winchester, England) 16(15): 1-100	- Systematic review used to identify primary papers
Turnbull, Sophie, Lucas, Patricia J, Redmond, Niamh M et al. (2018) What gives rise to clinician gut feeling, its influence on management decisions and its prognostic value for children with RTI in primary care: a prospective cohort study. BMC family practice 19(1): 25	- Does not report on a risk assessment tool *Secondary publication of the TARGET trial. Does not present a risk assessment tool; reports on symptoms associated with clinician 'gut feeling' and how this is associated with referral for same day hospital admission*
Van den Bruel, Ann, Aertgeerts, Bert, Bruyninckx, Rudi et al. (2007) Signs and symptoms for diagnosis of serious infections in children: a prospective study in primary care. The British journal of general practice : the journal of the Royal College of General Practitioners 57(540): 538-46	- Excluded population *Population was children with serious infection (sepsis, meningitis, cellulitis etc) and only a very small proportion had pneumonia (16 out of 3981 patients). Tool was for identifying signs of serious infection in children; not pneumonia specific*
van Houten, Chantal, van de Maat, Josephine Sophia, Naaktgeboren, Christiana et al. (2019) Update of a clinical prediction model for serious bacterial infections in preschool children by adding a host-protein-based assay: a diagnostic study. BMJ paediatrics open 3(1): e000416	- Outcome to be predicted do not match that specified in the protocol *Looked at use of Feverkidstool to predict diagnosis of pneumonia or other serious bacterial infections. Did not report on the use of the tool for making decisions about hospitalisation*
van Ierland, Yvette, Elshout, Gijs, Berger, Marjolein Y et al. (2015) Translation of clinical prediction rules for febrile children to primary care practice: an observational cohort study. The British journal of general practice : the journal of the Royal College of General Practitioners 65(633): e224-33	- Excluded population *Validation of Van den Bruel tool but in a population of febrile children - not specific to pneumonia and no data for pneumonia-only subsample reported.*
Verbakel, J.Y., Lemiengre, M.B., De Burghgraeve, T. et al. (2014) Diagnosing serious infections in acutely ill children in ambulatory care (ERNIE 2 study protocol, part A): Diagnostic accuracy of a clinical decision tree and added value of a point-of-care C-reactive protein test and oxygen saturation. BMC Pediatrics 14(1): 207	- Trial protocol

Study	Reason
Verbakel, Jan Y, Lemiengre, Marieke B, De Burghgraeve, Tine et al. (2015) Validating a decision tree for serious infection: diagnostic accuracy in acutely ill children in ambulatory care. BMJ open 5(8): e008657	- Excluded population *External validation of an excluded tool for use with children suspected of serious bacterial infection - not specific to pneumonia*
Verbakel, Jan Y, Van den Bruel, Ann, Thompson, Matthew et al. (2013) How well do clinical prediction rules perform in identifying serious infections in acutely ill children across an international network of ambulatory care datasets?. BMC medicine 11: 10	- Outcome to be predicted do not match that specified in the protocol *Looked a clinical prediction rules for identifying serious bacterial infections - outcome was diagnosis rather than hospitalisation, and were not pneumonia-specific.*
Williams, Derek J. Zhu, Yuwei Grijalva, Carlos G. Self, Wesley H. Harrell, Frank E., Jr. Reed, Carrie Stockmann, Chris Arnold, Sandra R. Ampofo, Krow K. Anderson, Evan J. Bramley, Anna M. Wunderink, Richard G. McCullers, Jonathan A. Pavia, Andrew T. Jain, Seema Edwards, Kathryn M. (2016) Predicting Severe Pneumonia Outcomes in Children. PEDIATRICS 138(4)	- Outcome to be predicted do not match that specified in the protocol *Pneumonia severity assessment tool for predicting risk of poor outcomes in children hospitalised with pneumonia (e.g. need for ICU admission, IMV). Not for use in primary care to support decisions about hospitalisation.*

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

Study	Code [Reason]
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*
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 check 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 study*

Study	Code [Reason]
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 United Kingdom: A Cost-Utility Analysis. PharmacoEconomics - open 6(1): 73-83	- Study does not contain a relevant intervention *Continuous monitoring versus intermittent monitoring, NEWS used in both arms*
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 pneumonia (CAP) in the UK, France and Spain. BMC pulmonary medicine 23(1): 220	- Not a relevant study design *Cost consequence study*

Study	Code [Reason]
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 Cohort Study. Evidence-based complementary and alternative medicine : eCAM 2019: 4510591	- Study does not contain a relevant intervention *Andrographolide Sulfonate injection*
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)*

Study	Code [Reason]
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*
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	Included in review question 4.2
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*

Appendix K– Research recommendations – full details

K1.1 Research recommendation

In children presenting to primary care with signs or symptoms of pneumonia, what is the most accurate and cost-effective clinical prediction tool to identify under 18s who require referral to secondary care for assessment, treatment and admission?

K1.1.1 Why this is important

The evidence on risk assessment tools and clinical prediction rules for identifying children attending primary care who may be at risk of deterioration was very limited and the committee were not able to make recommendations about tools that can support decision making about referral to secondary care. Some tools exist that can be used to identify children at low risk of future deterioration and for whom antibiotics are not required, but the is no currently available tool to reliably identify children at high risk of future deterioration and who need referral to secondary care.

K1.1.2 Rationale for research recommendation

Importance to 'patients' or the population	Large numbers of children present to primary care with respiratory tract infection symptoms and while most will not require antibiotics and can be safely cared for at home, a small number can quickly deteriorate and require secondary care. Identifying those most at risk is important to ensure children do not become seriously unwell, as well as preventing over-referral of children to hospital.
Relevance to NICE guidance	There are recommendations about referral to hospital or GP-led care for adults but no recommendations for children about when they should be referred for hospital assessment. This is a gap in the guideline.
Relevance to the NHS	Primary care practitioners have highlighted a need for a simple, effective tool to support decision making in this area. Primary consultations for children with LRTI symptoms are very high and this would help to manage that workload effectively.
National priorities	Low
Current evidence base	Some limited evidence. STARWAVe tool exists but is not externally validated for use in decisions about referral to secondary care. Development of new models may be useful.
Equality considerations	Babies are at high risk of developing serious illness, and pneumonia is more common in children under 5.

K1.1.3 Modified PICO table

Population	Babies, children and young people presenting to primary care with signs and symptoms suggestive of pneumonia
Intervention	Risk assessment or clinical prediction tools that use a collection of respiratory and fever based symptoms or prediction model based on a collection of symptoms.
Comparator	N/A
Outcome	• Admission to hospital • Admission to ICU • Length of hospital stay • Re-presentation to primary care • Cost effectiveness
Study design	Prospective cohort studies External validation studies
Timeframe	1 month
Additional information	None