National Institute for Health and Care Excellence

Acute Respiratory Infection in over 16s: Initial assessment and management

[A] Evidence review for signs, symptoms and early warning scores for predicting severe illness in the initial assessment of people with suspected acute respiratory infection

NICE guideline XXX

Evidence review to underpin recommendations and research recommendations in the NICE guideline

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Evidence Review

developed by the York Evidence Synthesis (YES) Group

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1 Initial assessment and management of people aged 16 years or over with suspected acute respiratory infection

1.1 Review question

In people aged 16 years or over with suspected acute respiratory infection (ARI):

1. What are the signs, symptoms and early warning scores (EWS) that have been evaluated?

2. What are the strategies for the triage of patients (for example, applying clinical prediction rules using signs, symptoms, EWS thresholds) to avoid serious illness?

1.1.1 Introduction

Before the COVID-19 pandemic, people with suspected ARI either presented to NHS 111 or primary care for assessment and management, with more severe cases referred for hospital assessment, or they presented directly to an emergency department or to the ambulance service if their symptoms were more serious. Since the pandemic, the levels of ARI (particularly pneumonia caused by COVID-19 infection) have increased. In response to this the NHS has set up a number of ARI hubs and ARI virtual wards to relieve pressure on other parts of the local healthcare system.

For people aged 16 and over with suspected ARI, initial consultations with the health system may occur remotely (for example, through online apps, email exchange or text message, via telephone through NHS 111 or with a GP, via video call, or direct to 999 emergency call centres) or face-to-face (for example, in the person's home or care home, in primary care including community pharmacy or ARI hubs, in NHS walk-in centres, and in emergency departments). Those with suspected ARI can be advised to remain at home for self-monitoring (with or without being prescribed antibiotics or antivirals), referred to ARI virtual wards for further monitoring, or referred to, and/or admitted to, a hospital.

NICE has been asked to produce a number of related products to support and inform the expansion of virtual ward provision and other intermediate care areas. This review focuses on the early assessment of people aged 16 and over with suspected ARI in remote and face-to-face settings. Evidence on the use of signs, symptoms and EWS, either individually or in combination, to identify serious cases or predict potential to deteriorate (which would require a different level of monitoring and healthcare) will be reviewed. This will inform the development of a NICE guideline intended to aid healthcare professionals in deciding whether to refer people aged 16 and over with suspected ARI, including referrals to virtual wards and ARI hubs.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	People aged 16 years or over with suspected ARI (including bronchitis, common cold, glandular fever, influenza, laryngitis, sore throat (pharyngitis and tonsillitis), pneumonia and severe acute respiratory syndrome (SARS)). Exclusion criteria: People aged 16 or over with a confirmed COVID-19 diagnosis, who are hospital in-patients, who have a respiratory infection during end-of-life care, and those with aspiration pneumonia, bronchiectasis, cystic fibrosis, or known immunosuppression.
Phenomenon of interest	Symptoms, signs and externally validated EWS for the assessment of suspected ARI, including: cough, coughing up blood, purulent sputum, malaise, coryza, temperature/signs of fever, sore throat, hoarse voice, breathlessness and/or increased respiratory rate, wheeze/chest tightness, cyanosis, loss of appetite, lethargy, agitation, confusion, delirium, drowsiness, headache, rigors, chest pain, monitoring parameters based on digital technologies where available (e.g. pulse oximetry, peak flow), sudden deterioration in any of the above, EWS (including NEWS/NEWS2, CRB65/CURB65, CENTOR criteria), and any combination of the above.

Outcomes	Assessed within 4 weeks of consultation:
	• Hospital admission
	• Escalation of care to any setting including:
	  ○ Face to face consultation
	  ○ Re-consultation/appointment
	  ○ Virtual ward
	  ○ Referral to ARI hub
	  ○ A&E visit
	  ○ Unplanned hospital admission
	• Hospital length of stay
	• Follow-up consultation/ongoing monitoring
	• Antibiotic/antiviral use
	• Time to clinical cure/resolution of symptoms
	• Mortality
	Secondary outcomes:
	• Patient acceptability
	• Patient preference
	• HRQoL (using a validated scale)

Study type	Systematic reviews.

For the full protocol see Appendix A – Review protocol.

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 – Review protocol and the methods document.

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

1.1.3.1 Search methods

Clinical studies

The aim of the search was to identify systematic reviews relating to the assessment of signs and symptoms, early warning scores or strategies for triage in people with suspected acute respiratory infection. A search strategy was designed in Ovid MEDLINE by an information specialist in consultation with the review team. The strategy was comprised of terms for respiratory infections combined (using the Boolean operator AND) with terms for the assessment of signs and symptoms, early warning scores or triage strategies. Text word searches in the title and abstract fields of records were included in the strategy along with relevant subject headings. A summary of search filters and limits applied to the search can be found in Table 2 below. The MEDLINE strategy was checked by a second information specialist using aspects of the PRESS checklist.[1] The final MEDLINE strategy was adapted for use in all databases searched.

The following databases were searched on 15th May 2023: MEDLINE ALL (Ovid), Embase (Ovid), and the Cochrane Database of Systematic Reviews (Wiley). 5494 records were retrieved in total and imported into EndNote 20 for deduplication. After duplicates were removed 3621 records remained for screening.

Table 2: Database parameters, filters and limits applied.

Database	Dates searched	Search filter and limits applied
MEDLINE via Ovid	1946 – 11th May 2023	Systematic reviews Exclusions (animal studies, letters, comments, editorials, news) English language
Embase via Ovid	1974 – 12th May 2023	Systematic reviews Exclusions (animal studies, letters, editorials, notes, conference abstracts, preprints) English language
Cochrane Database of Systematic Reviews via the Cochrane Library, Wiley	Issue 5 of 12, May 2023	None

Economic evaluations

The aim of the search was to identify economic evaluations relating to the assessment of signs and symptoms, early warning scores or strategies for triage in people with suspected acute respiratory infection. A search strategy was designed in Ovid MEDLINE by an information specialist (MH) in consultation with the review team. The strategy was comprised of terms for respiratory infections combined (using the Boolean operator AND) with terms for the assessment of signs and symptoms, early warning scores or triage strategies. Text word searches in the title and abstract fields of records were included in the strategy along with relevant subject headings. The final MEDLINE strategy was adapted for use in all databases searched by another Information Specialist (HF). A summary of search filters and limits applied to the search can be found in Table 3 below.

The following databases were searched on 15th May 2023: MEDLINE ALL (Ovid), Embase (Ovid), EconLit (Ovid), and NHS EED (CRD). 3633 records were retrieved in total and imported into EndNote 20 for deduplication. After duplicates were removed 2622 records remained for screening.

Table 3: Database parameters, filters and limits applied.

Database	Dates searched	Search filter and limits applied
MEDLINE via Ovid	1946 – 11th May 2023	Economic Evaluations Exclusions (animal studies, letters, comments, editorials, news) English language
Embase via Ovid	1974 – 12th May 2023	Economic Evaluations Exclusions (animal studies, letters, editorials, notes, conference abstracts, preprints) English language
EconLit via Ovid	1886 – 27th April 2023	N/A
NHS EED via CRD	Inception – 31st March 2015	N/A

1.1.4 Clinical evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 3621 references, after deduplication between databases (see Appendix B for the literature search strategy).

These 3621 references were screened at title and abstract level against the review protocol, with 3494 excluded at this level. The study selection process was initially piloted on 73 (2%) of the references to check consistency in screening decisions between reviewers. 10% of

references were screened separately by two reviewers and discrepancies were resolved by discussion.

The full texts of 127 reviews were ordered for closer inspection. Nine of these studies met the criteria specified in the review protocol (Appendix A). For a summary of the nine included studies see Table 4. All full texts were screened independently by two reviewers and discrepancies were resolved by discussion.

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

See Section 1.1.12 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 K – Excluded studies.

1.1.5 Summary of studies included in the clinical evidence

The included study characteristics are summarised in Table 4 below.

Table 4: Summary of studies included in the evidence review

Study details	Population	Setting	Prognostic factors/ Prognostic model(s)	Outcomes	Risk of bias
Individual signs/symptoms and Centor score for adults presenting with sore throat symptoms					
Aalbers (2011)[2] Systematic review including 21 studies	Adults (≥15 years of age) presenting with sore throat symptoms	Primary care and the emergency department (USA, Canada, Europe, New Zealand, Thailand, Israel)	Individual signs and symptoms (absence of cough, fever, anterior cervical adenopathy, tender anterior cervical adenopathy, any exudates) and Centor score	Usefulness of individual signs and symptoms in assessing the risk of streptococcal pharyngitis and diagnostic accuracy of the Centor score as a decision rule for antibiotic treatment	Low
Early warning scores (EWS) for patients with community acquired pneumonia (CAP)					
Akram (2011)[3] Systematic review including 13 studies	Outpatients with community acquired pneumonia (CAP)	Outpatients; either exclusively managed in the community or discharged from an emergency department <24 hours after admission (USA, Canada, Netherlands, Germany, Spain, France, UK)	CRB65, CURB65 and Pneumonia Severity Index (PSI)	Outpatient mortality and diagnostic accuracy	Low
Chalmers (2011)[4] Systematic review including 6 studies	Outpatients with CAP	Emergency department and walk-in medical centre (USA, Canada, Spain, France)	PSI and other criteria for assessing severity/requirement for in-patient care	Proportion of patients treated as outpatients, mortality, hospital re-admissions, health related quality of life, return to usual activities and patient satisfaction with care.	Low
Ebell (2019)[5] Systematic review including 29	Patients with CAP	The review included hospitalised patients, ambulatory patients and	CRB-65	Prediction of mortality	High

Study details	Population	Setting	Prognostic factors/ Prognostic model(s)	Outcomes	Risk of bias
studies; 15 were in emergency department or primary care settings (update of McNally 2010)		both; the 15 studies that included patients in emergency department or primary care settings are relevant to this review (most studies from Europe)			
McNally (2010)[6] Systematic review including 14 studies; 4 included community-based patients	Adults (≥16 years of age) with a primary diagnosis of CAP	The review included hospitalised patients, primary care patients and patients treated as outpatients; the 4 studies that included primary care patients and patients treated as outpatients are relevant to this review (study location not reported)	CRB-65	30-day mortality	Low
Metlay (2019)[7] Systematic review including 7 studies relating to the question of interest	Adults diagnosed with CAP	Inpatient versus outpatient treatment location (study location not reported)	PSI and CURB-65	Initial site of treatment	High
Nannan Panday (2017)[8] Systematic review including 42 studies; 4 included patients with CAP or	Adults (≥16 years of age) at the emergency department or acute medical unit	Emergency department and acute medical unit (Denmark, Netherlands, Norway, Germany, Hong Kong, Ireland, Israel, Italy, Singapore, South Africa, South Korea, Sri Lanka, Sweden, Switzerland,	25 different types of early warning score (EWS). For the 4 studies relevant to our question, the scores assessed were Chronic Respiratory Early Warning Score (CREWS), CRB-65, CURB-65, National Early Warning Score (NEWS)*, PSI, Systemic	Prediction of mortality and/or intensive care unit (ICU) admission	Low

Study details	Population	Setting	Prognostic factors/ Prognostic model(s)	Outcomes	Risk of bias
respiratory distress		Turkey, UK, USA and Vietnam)	Inflammatory Response Syndrome (SIRS), Standardised Early Warning Score (SEWS) and Salford National Early Warning Score (S-NEWS)		
Smith (2021)[9] Systematic review including 38 studies relating to the question of interest	Adult emergency department patients diagnosed with CAP	Emergency department (USA, Spain, Switzerland, Australia, Canada, China, France, Japan, Korea, Turkey, UK and Europe, where reported)	PSI and CURB-65 for predicting mortality. 5 clinical decision aids for predicting the need for ICU admission: American Thoracic Society (ATS) 2001, Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) 2007, Severe CAP (SCAP/CURXO-80), SMART-COP, Risk of Early Admission to the ICU (REA-ICU)	Prediction of mortality (PSI and CURB-65) and prediction of need for ICU admission (ATS 2001, IDSA/ATS 2007, SCAP/CURXO-80, SMART-COP and REA-ICU)	Unclear
Early warning scores (EWS) for patients with nursing home acquired pneumonia (NHAP)					
Dosa (2005)[10] Systematic review including 3 studies relating to the question of interest	Nursing home residents with nursing home acquired pneumonia (NHAP)	Nursing homes (USA)	PSI, a 5-point scale developed by Naughton and Mylotte and an 8-variable model developed by Mehr et al.	Prediction of mortality	High

Abbreviations: ATS = American Thoracic Society; CAP = community acquired pneumonia; EWS = early warning scores; ICU = intensive care unit; IDSA/ATS = Infectious Diseases Society of America/American Thoracic Society; MEDS = Mortality in Emergency Department Sepsis score; MEWS = Modified Early Warning Score; NEWS = National Early Warning Score; NHAP = nursing home acquired pneumonia; PSI = Pneumonia Severity Index; REA-ICU = Risk of Early Admission to the ICU; REMS = Rapid Emergency Medicine Score; SCAP = Severe CAP.

* NEWS was updated to NEWS2 in December 2017, after the Nannan Panday review was published.

See Appendix D – Clinical evidence for full evidence tables. Appendix E – Early warning scores assessed presents the early warning scores (EWS) assessed in the included studies. Appendix G – ROBIS risk of bias assessment results presents the ROBIS risk of bias assessment results.

1.1.6 Summary of the clinical evidence

1.1.6.1 Individual signs/symptoms and the Centor score for adults presenting with sore throat symptoms

One systematic review assessed the usefulness of individual signs and symptoms in assessing the risk of streptococcal pharyngitis, and the diagnostic accuracy of the Centor score as a decision rule for antibiotic treatment, in adults (≥15 years) presenting to primary care (19 studies) or the emergency department (2 studies) with symptoms of sore throat.[2] The review, published in 2011, included 21 diagnostic accuracy studies from the USA, Canada, Europe, New Zealand, Thailand and Israel that were published between 1975 and 2008; the overall quality of the included studies was considered to be good. The prevalence of Group A β-haemolytic streptococcal (GABHS) pharyngitis varied widely between studies, ranging from 4.7% to 37.6%. All 21 studies (n=4,839 patients) reported data on signs and symptoms and 15 studies (n=2,900 patients) reported data on the Centor score. Individual signs and symptoms assessed were: absence of cough, fever, anterior cervical adenopathy, tender anterior cervical adenopathy and any exudates (tonsillar exudate, pharyngeal exudate or any exudate). The reference standard was throat culture. Summary diagnostic accuracy results (sensitivity, specificity, positive and negative likelihood ratios) are presented in Appendix D – Clinical evidence.

The authors concluded that individual symptoms and signs have only a modest ability to rule in or out a diagnosis of GABHS pharyngitis. They concluded that the Centor score (cut-off score of ≥3) has reasonably good specificity and can enhance the appropriate prescribing of antibiotics, but should be used with caution in settings with a low prevalence of GABHS pharyngitis, such as primary care. This review had a low risk of bias and the conclusions appear to be appropriate.

1.1.6.2 Early warning scores (EWS) for patients with community acquired pneumonia (CAP)

Seven systematic reviews assessed EWS for patients with community acquired pneumonia (CAP),[3-9] primarily for the prediction of mortality and/or to determine the site of treatment (inpatient versus outpatient care or requirement for intensive care unit admission). Full details are presented in Appendix D – Clinical evidence. The most commonly assessed EWS were the Pneumonia Severity Index (PSI; 4 reviews),[3, 4, 7, 9] CRB-65 (3 reviews)[3, 5, 6] and CURB-65 (3 reviews).[3, 7, 9] One review assessed a range of EWS; those assessed in the subgroup of studies of patients with CAP or respiratory distress were the Chronic Respiratory Early Warning Score (CREWS), CRB-65, CURB-65, National Early Warning Score (NEWS), PSI, Systemic Inflammatory Response Syndrome (SIRS), Standardised Early Warning Score (SEWS) and Salford National Early Warning Score (S-NEWS).[8] None of the reviews assessed NEWS2; NEWS was updated to NEWS2 in December 2017, after the Nannan Panday review was published. The setting of the included studies included primary care, walk-in medical centre, emergency department, and acute medical unit; most of the included studies were from the USA, Canada and Europe, where stated, and they were published between 1997 and 2018. Study quality was assessed using a range of different tools with variable results; many of the included studies were considered to have significant limitations/a moderate to high risk of bias. One review[5] was an update of another of the included reviews.[6] There was a great deal of overlap in included primary studies between the

reviews; Table 5 shows the eleven studies that were included in more than one of the reviews.

Table 5: Primary studies included in more than one review

Included studies	Akram, 2011	Chalmers, 2011	Ebell, 2019	McNally, 2010	Metlay, 2019	Nannan Panday, 2017	Smith, 2021
Atlas, 1998	●	●			●		●
Bauer, 2006	●		●	●			
Bont, 2008	●		●	●			
Capelastegui, 2006	●		●	●			●
Carratala, 2005	●	●					●
Fine, 1997	●						●
Julian-Jiminez, 2013					●		●
Kruger, 2008			●	●			
Marrie, 2000		●			●		●
Renaud, 2007	●	●			●		
Yealy 2005	●	●			●		●

Two systematic reviews had a low risk of bias and good applicability to the review question.[3, 6] Two had a low risk of bias, but poorer applicability as the risk scoring system was only one component of the interventions assessed[4] or the population also included patients with suspected exacerbation of chronic obstructive pulmonary disease (COPD).[8] One review had an unclear risk of bias as there was limited methodological detail reported, but good applicability.[9] Two reviews had a high risk of bias, owing to a limited search strategy and/or poor reporting with limited details of the included studies.[5, 7] The reviews judged to be at low risk of bias, assessed using the ROBIS tool,[11] were considered to be good quality.

A good quality systematic review, published in 2011, concluded that patients in low risk PSI and CRB-65 classes were found to be at low risk of death when managed as outpatients, but that further studies are needed in out-patient cohorts; this review included studies of patients managed exclusively in the community or discharged from an emergency department within 24 hours.[3] Another good quality review, published in 2010, concluded that the CRB-65 has not been validated sufficiently in primary care settings and preliminary findings suggest over-prediction, so it's value as a prognostic indicator in the community remains unclear.[6]

A good quality review published in 2017 concluded that MEWS and NEWS generally had favourable results in the emergency department or acute medical unit setting for all endpoints; for mortality prediction NEWS was the most accurate score in those with respiratory distress.[8] Intensive care unit (ICU) admission was best predicted with NEWS. The authors stated that future studies should concentrate on a simple and easy to use prognostic score such as NEWS with the aim of introducing this throughout the (pre-hospital and hospital) acute care chain.

The final good quality systematic review, with poorer applicability due to the risk scoring system being only one component of the interventions assessed, concluded that strategies to increase the proportion of patients treated in the community are safe, effective and acceptable to patients.[4]

A review with an unclear risk of bias, published in 2021, including patients in an emergency department setting, concluded that the PSI and CURB-65 are both well-validated clinical decision aids that can predict short-term mortality in patients with CAP and can be used to identify low-risk patients for whom outpatient management may be considered.[9] The authors stated that both aids are appropriate for this purpose in the emergency care setting; the PSI appears to be slightly better at identifying low-risk patients, but requires data from a greater number of tests, including some not routinely conducted in the emergency department. They further stated that for decisions regarding ICU admission, clinical decision aids designed for this purpose (such as the IDSA/ATS 2007) should be considered superior to the PSI and CURB-65.

One of the reviews with a high risk of bias, which included patients in emergency department and primary care settings, concluded that the CRB-65 can be used by physicians to estimate mortality risk and can serve as a useful check on physician judgement; patients in the low-risk group with a score of 0 have a very low mortality risk and can in most cases safely be treated as outpatients, whilst most patients in the moderate- and high-risk groups should be hospitalised (although other considerations may alter these decisions regarding treatment setting).[5] The other review with a high risk of bias recommended that clinicians use a validated clinical prediction rule for prognosis, in addition to clinical judgement, to determine the need for hospitalisation; preferentially the PSI over the CURB-65.[7]

In summary, it appears that further research is needed to validate the PSI and CRB-65 in primary care/community settings. However, the PSI requires data from a large number of tests, some of which are not routinely conducted in primary care/community settings. The PSI and CURB-65 appear to be useful for predicting short-term mortality and identifying low-risk patients who may be considered for outpatient management when used in an emergency department setting; although some tests required for the PSI may not be routinely conducted in an emergency department setting (such as arterial blood gases). NEWS and MEWS appear to be useful in an emergency department or acute medical unit setting for predicting mortality and NEWS was useful for predicting need for ICU admission. The ATS 2001 and IDSA/ATS 2007 appear to be superior to the PSI and CURB-65 for decisions regarding ICU admission.

1.1.6.3 Early warning scores (EWS) for patients with nursing home acquired pneumonia (NHAP)

One systematic review with a high risk of bias assessed the PSI, a 5-point scale developed by Naughton and Mylotte and an 8-variable model developed by Mehr et al. for predicting mortality in nursing home residents with nursing home acquired pneumonia (NHAP).[10] Three studies, conducted between 1998 and 2001 in USA nursing homes, related to the question of interest; one study assessed each EWS. The review does not appear to have assessed the quality of the included studies. The authors concluded that there are numerous problems with using current models in clinical practice, such as the fact that mortality prediction models are generally age-driven, therefore, as nursing home residents are generally very old, this eliminates one of the most discriminating features of the probability model. Prediction models do not incorporate the resident's end-of-life wishes or overall goals of care. Current models for predicting mortality require data collection that is often not readily available at the time that triage decisions need to be made. Whilst the issues discussed appear to be relevant considerations when assessing the use of EWS in a nursing home setting, the review was poorly conducted and reported, and it is unclear whether relevant studies were missed and whether the included studies were valid.

1.1.7 Economic evidence

This section provides an overview of existing cost-effectiveness evidence relating to the assessment of signs and symptoms, early warning scores or strategies for triage in people with suspected acute respiratory infection.

The bibliographic search detailed in Section 1.1.3.1 was used to identify relevant studies. This review considered a range of economic studies including modelling studies and trial-based economic evaluations. The inclusion criteria considered full economic evaluations comparing two or more alternative interventions in terms of both costs and consequences. Only cost-effectiveness, cost-utility, cost-benefit, and cost-minimisation analyses were considered for inclusion.

1.1.7.1 Included studies

The initial search identified a total of 2,622 references after deduplication between databases (see Appendix B – Literature search strategies for the literature search strategy), which were subsequently screened at title and abstract level against the review protocol. The study selection process was initially piloted on 10% (263) of total references for consistency between reviewers, with the remaining references independently screened by two reviewers and any disagreements resolved by consensus. A total of 13 studies were identified as potentially relevant from their title and abstract. Full-text papers of the 13 references were subsequently ordered for assessment and screened by the two reviewers, with any discrepancies resolved by consensus. Only one of these studies, summarised in Table 6, met the criteria specified in the review protocol (see Appendix I – Economic evidence tables for the economic evidence table).[12]

A PRISMA diagram of the study selection process is presented in Appendix H – Economic evidence study selection.

1.1.7.2 Excluded studies

Of the 13 studies identified as potentially relevant from their title and abstract, 12 studies were excluded as they did not meet the review criteria based on population, intervention, or study design. Details of excluded studies at full text and reasons for exclusion are summarised in Appendix K – Excluded studies.

1.1.8 Summary of studies included in the economic evidence

Table 6: Economic evidence profile

Study details	Applicability	Limitations	Other comments	Costs (£)	Effects (QALYs)	ICER	Uncertainty
Little et al. 2014 (UK)[12]	Partially applicable	Minor limitations. This study is only partially relevant to the review question, but highlights the possible impact of using symptoms to assess short term ARI conditions.	• Cost-utility analysis • Cost-effectiveness analysis • Population: Patients aged ≥ 3 years and had acute sore throat • Comparators: 1. Clinical scores (FeverPAIN) 2. Rapid antigen detection tests (RADTs) 3. Delayed antibiotic prescribing (DP)	Total costs at 14 and 28-days (95% CI): - DP: £49.70 (43.30 to 56.00) - FeverPAIN: £45.90 (41.50 to 50.20) - RADT: £48.50 (45.00 to 52.00)	Cost-utility analysis (outcome measure: quality adjusted life years (QALYs)) 14-day period (95% confidence interval (CI)): - DP: 0.0057 (0.0044 to 0.007) - FeverPAIN: 0.0058 (0.0045 to 0.0071) - RADT: 0.00584 (0.0046 to 0.0071) 28-day period (95% CI): - DP: 0.0171 (0.0131 to 0.0211) - FeverPAIN: 0.01741 (0.0135 to 0.0213) - RADT: 0.01752 (0.0138 to 0.0212	Cost-utility analysis -DP is dominated (more costly and less clinically effective) by FeverPAIN and RADT. -Compared to FeverPain, RADT generates an incremental cost effectiveness ratio (ICER) of £74,286 and £24,528 at 14 and 28 days respectively. Cost-effectiveness analysis -DP is dominated (more costly and	Cost-effectiveness acceptability curves indicated considerable uncertainty, particularly around the QALY estimate. At a threshold of £30,000 per QALY, the probabilities that delayed prescribing, clinical score and RADT are the most cost-effective option were 25%, 40% and 35% respectively, for the 14-day period, and 28%, 38% and 35%,

Study details	Applicability	Limitations	Other comments	Costs (£)	Effects (QALYs)	ICER	Uncertainty
					Cost-effectiveness analysis (outcome measure: symptom score) -DP: 3.15 (2.93 to 3.37) -FeverPAIN: 2.83 (2.61 to 3.05) - RADT: 2.84 (2.62 to 3.07)	less clinically effective) by FeverPAIN and RADT. -RADT is dominated (more costly and less clinically effective) by FeverPAIN	respectively, for the 28-day period.

Abbreviations: CI = confidence interval; DP = delayed antibiotic prescribing; ICER = incremental cost effectiveness ratio; QALY = quality adjusted life years; RADT = rapid antigen detection test.

1.1.9 Summary of the economic evidence

Limited relevant cost-effectiveness evidence was identified with only one study included in the cost-effectiveness review. While the study satisfied the review criteria regarding the population and study design, it only partially met the criteria concerning the intervention because it involved evaluating a diagnostic strategy in addition to examining a clinical symptom score. Nonetheless, by examining a clinical score in conjunction with standard care, the study might offer insights into the potential cost-effectiveness of implementing a clinical score-based approach for the triage of ARIs.

The identified study, Little et al. (2014),[12] utilised outcomes from the PRImary care Streptococcal Management (PRISM) randomized controlled trial which evaluated the clinical and cost-effectiveness of clinical scores and rapid antigen detection tests (RADT) for sore throats, compared to delayed (antibiotic) prescribing. The outcome measures assessed were clinical symptom score (based on the mean rating of sore throat and difficulty of swallowing for days 2 to 4) and EQ5D-3L scores (measured on day 14). These outcomes were respectively used in the reported cost-effectiveness and cost-utility analysis. Costs and resource use captured included those needed to directly provide the interventions (practitioner time and cost of test) as well as subsequent care costs. The latter included subsequent antibiotic acquisition administration costs, accident and emergency visits and inpatient hospitalisation costs.

Mean severity scores were lower in the clinical scores group compared to the delayed prescribing group; -0.33 (95% CI –0.64 to –0.02). A similar reduction was also observed in the RADT group; –0.30 (95% CI –0.61 to 0.004) compared to delayed prescribing. The authors commented that this is equivalent to one in three patients rating sore throat severity as slight rather than a moderately bad problem. The study found no statistically significant differences, with wide confidence intervals (CI), in quality adjusted life years (QALYs) gained among the three participant groups. This uncertainty may stem from the fact that the EQ5D scores were obtained from a smaller data set, which was not powered to reflect small differences in quality of life. Furthermore, QALYs were estimated from EQ5D scores captured on day 14. The authors noted that there is a possibility that a significant number of individuals could have already recovered before the day 14 assessment, resulting in their health returning to normal. As a result, the EQ5D scores at 14 days, and consequently the difference in QALYs, may not strongly correlate with changes in symptom scores. The authors also considered that EQ5D may not accurately capture changes in health-related quality of life due to its potential lack of sensitivity.

Differences in mean costs between the three groups were largely attributed to the first recruitment visit and duration of that visit. The duration of contact reported by general practitioners (GPs) was comparable between the delayed and clinical scores groups, but slightly longer in the RADT group. As a result of this disparity and the cost associated with the diagnostic test, RADT was associated with higher implementation costs compared to both the delayed prescribing and clinical symptom scores groups. The clinical scores and RADT groups were also associated with lower antibiotic prescription compared to the delayed group, resulting in cost savings relative to delayed prescribing.

The findings of this study indicated that, from a NHS perspective, clinical scores were likely to be the most cost-effective strategy compared to both RADT and delayed (antibiotic) prescribing.

The cost-effectiveness analysis found that clinical scores were more clinically effective and less costly than RADT. However, the difference in point estimates for symptom severity scores between clinical scores (2.83, 95% CI 2.61 to 3.05) and RADT (2.84, 95% CI 2.62 to

3.07) were marginal with overlapping CIs. Both clinical scores and RADT were found to dominate delayed prescribing, generating greater benefits at lower cost.

Although the cost-utility analysis demonstrated considerable uncertainty around the QALY estimates, the results suggested that clinical scores was the most likely to be cost-effective, particularly at lower willingness to pay thresholds. RADT was the most effective intervention in the cost-utility analysis, yielding marginally higher QALY gains than the clinical scores group. Resulting pairwise ICERs for RADT compared with clinical scores were £74,286 and £24,528 per QALY at 14 and 28 days follow up respectively. As per the cost-effectiveness analysis both clinical scores and RADT were found to dominate delayed prescribing, generating greater benefits at lower cost.

Quality assessment using NICE economic evaluations checklist suggested no significant methodological concerns.

1.1.10 Economic model

No economic modelling was undertaken for this review question.

1.1.11 Evidence statements

1.1.11.1 In people aged 16 years or over with suspected acute respiratory infection (ARI), what are the signs, symptoms and early warning scores (EWS) that have been evaluated?

Several EWS have been evaluated in people aged 16 years or over with suspected ARI: Centor, CRB-65, CURB-65, PSI, CREWS, NEWS, SIRS, SEWS, S-NEWS, ATS 2001, IDSA/ATS 2007, SCAP/CURXO-80, SMART-COP and REA-ICU. Nine systematic reviews addressed this research question; all assessed patients presenting in face-to-face settings (primary care, walk-in medical centre, emergency department, acute medical unit or nursing home) rather than remote settings. The most commonly assessed EWS were the PSI, CRB-65 and CURB-65.

1.1.11.2 In people aged 16 years or over with suspected acute respiratory infection (ARI), what are the strategies for the triage of patients (for example, applying clinical prediction rules using signs, symptoms, EWS thresholds) to avoid serious illness?

The evidence was insufficient to definitively answer this question.

Seven systematic reviews assessed EWS for predicting mortality and/or to determine the site of treatment for patients with community acquired pneumonia. There was a great deal of overlap in the primary studies included in the reviews and many of the primary studies were considered to have significant limitations.

Two reviews that assessed the CRB-65 (both good quality) concluded that further research is needed in community settings. One of these reviews also assessed the PSI; however, the PSI requires data from a large number of tests, some of which are not routinely conducted in community settings. One review (also good quality) concluded that NEWS appears to provide the most accurate score for predicting mortality and the need for ICU admission in patients with respiratory distress in an emergency department or acute medical unit setting.

One review (good quality) concluded that individual symptoms and signs (absence of cough, fever, anterior cervical adenopathy, tender anterior cervical adenopathy, any exudates) have only a modest ability to rule in or out a diagnosis of streptococcal pharyngitis in adults

presenting to primary care or the emergency department with sore throat. The review concluded that the Centor score (cut-off ≥3) has reasonably good specificity and can enhance the appropriate prescribing of antibiotics for streptococcal pharyngitis, but that it should be used with caution in low prevalence settings, such as primary care.

Only one review (poor quality) assessed the use of EWS (PSI and two other scores) for predicting mortality in nursing home residents with nursing home acquired pneumonia; the review concluded that there are numerous problems with using the scores in clinical practice.

The review of economic evidence identified a single study which indicated that clinical scores may be a cost-effective approach to triage patients compared with delayed prescribing. The study also offers insight into the cost-effectiveness of diagnostic testing in ARI scenarios. In this particular case, the findings indicated that there is no apparent advantage in incorporating diagnostic testing alongside clinical scores compared to using clinical scores alone. It is unclear whether the results obtained from managing a short-term condition (sore throat) are generalisable to the broader assessment of other ARI conditions.

1.1.12 Included studies

1.1.12.1 Clinical evidence

Aalbers J, O'Brien K K, Chan W S et al. Predicting streptococcal pharyngitis in adults in primary care: a systematic review of the diagnostic accuracy of symptoms and signs and validation of the Centor score. BMC Medicine 2011; 9:67

Akram A R, Chalmers J D and Hill A T. Predicting mortality with severity assessment tools in out-patients with community-acquired pneumonia. Q J Med 2011; 104:871-9

Chalmers J D, Akram A R and Hill A T. Increasing outpatient treatment of mild community-acquired pneumonia: systematic review and meta-analysis. European Respiratory Journal 2011; 37:858-64

Dosa D. Should I hospitalize my resident with nursing home-acquired pneumonia? Journal of the American Medical Directors Association 2005; 6:327-33

Ebell M H, Walsh M E, Fahey T et al. Meta-analysis of calibration, discrimination, and stratum-specific likelihood ratios for the CRB-65 score. Journal of General Internal Medicine 2019; 34: 1304-13

McNally M, Curtain J, O'Brien KK et al. Validity of British Thoracic Society guidance (the CRB-65 rule) for predicting the severity of pneumonia in general practice: systematic review and meta-analysis. British Journal of General Practice 2010; 60:e423-33

Metlay J P, Waterer G W, Long A C et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. American Journal of Respiratory & Critical Care Medicine 2019; 200:e45-67

Nannan Panday R S, Minderhoud T C, Alam N and Nanayakkara P W B. Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): A narrative review. European Journal of Internal Medicine 2017; 45:20-31

Smith M D, Fee C, Mace S E et al. Clinical policy: critical issues in the management of adult patients presenting to the emergency department with community-acquired pneumonia. Annals of Emergency Medicine 2021; 77:e1-e57

1.1.12.2 Economic evidence

Little P, Hobbs FD, Moore M, Mant D, Williamson I, McNulty C, et al. PRImary care Streptococcal Management (PRISM) study: in vitro study, diagnostic cohorts and a pragmatic adaptive randomised controlled trial with nested qualitative study and cost-effectiveness study. Health Technol Assess. 2014;18(6): 1-101

1.1.13 References

1. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 guideline statement. *J Clin Epidemiol* 2016;**75**:40-6. https://doi.org/10.1016/j.jclinepi.2016.01.021
2. Aalbers J, O'Brien KK, Chan WS, Falk GA, Teljeur C, Dimitrov BD*, et al.* Predicting streptococcal pharyngitis in adults in primary care: a systematic review of the diagnostic accuracy of symptoms and signs and validation of the Centor score. *BMC Med* 2011;**9**:67. https://dx.doi.org/10.1186/1741-7015-9-67
3. Akram AR, Chalmers JD, Hill AT. Predicting mortality with severity assessment tools in out-patients with community-acquired pneumonia. *QJM* 2011;**104**:871-9. https://dx.doi.org/10.1093/qjmed/hcr088
4. Chalmers JD, Akram AR, Hill AT. Increasing outpatient treatment of mild community-acquired pneumonia: systematic review and meta-analysis. *Eur Respir J* 2011;**37**:858-64. https://dx.doi.org/10.1183/09031936.00065610
5. Ebell MH, Walsh ME, Fahey T, Kearney M, Marchello C. Meta-analysis of calibration, discrimination, and stratum-specific likelihood ratios for the CRB-65 score. *J Gen Intern Med* 2019;**34**:1304-13. https://dx.doi.org/10.1007/s11606-019-04869-z
6. McNally M, Curtain J, O'Brien KK, Dimitrov BD, Fahey T. Validity of British Thoracic Society guidance (the CRB-65 rule) for predicting the severity of pneumonia in general practice: systematic review and meta-analysis. *Br J Gen Pract* 2010;**60**:e423-33. https://dx.doi.org/10.3399/bjgp10X532422
7. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K*, et al.* Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019;**200**:e45-67. https://dx.doi.org/10.1164/rccm.201908-1581ST
8. Nannan Panday RS, Minderhoud TC, Alam N, Nanayakkara PWB. Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): a narrative review. *Eur J Intern Med* 2017;**45**:20-31. https://dx.doi.org/10.1016/j.ejim.2017.09.027
9. Smith MD, Fee C, Mace SE, Maughan B, Perkins JC, Kaji A*, et al.* Clinical policy: Critical issues in the management of adult patients presenting to the emergency department with community-acquired pneumonia. *Ann Emerg Med* 2021;**77**:e1-57. https://dx.doi.org/10.1016/j.annemergmed.2020.10.024
10. Dosa D. Should I hospitalize my resident with nursing home-acquired pneumonia? *J Am Med Dir Assoc* 2005;**6**:327-33.
11. Whiting P, Savović J, Higgins JPT, Caldwell DM, Reeves BC, Shea B*, et al.* ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol* 2016;**69**:225-34. https://doi.org/10.1016/j.jclinepi.2015.06.005
12. Little P, Hobbs FD, Moore M, Mant D, Williamson I, McNulty C*, et al.* PRImary care Streptococcal Management (PRISM) study: in vitro study, diagnostic cohorts and a pragmatic adaptive randomised controlled trial with nested qualitative study and cost-effectiveness study. *Health Technol Assess* 2014;**18**:1-101. https://dx.doi.org/10.3310/hta18060

Appendices

Appendix A – Review protocol

Review protocol for acute respiratory infection in adults over 16 years: initial assessment and management

ID	Field	Content
0.	PROSPERO registration number	To be completed following sign off if appropriate.
1.	Review title	The clinical utility of signs, symptoms and early warning scores, either individually or in combination, for predicting severe illness in the initial assessment of people aged 16 years or over with suspected acute respiratory infection: a rapid evidence synthesis.
2.	Review question	RQ 1. In people aged 16 years or over with suspected acute respiratory infection (ARI): 1. What are the signs, symptoms and early warning scores (EWS) that have been evaluated? 2. What are the strategies for the triage of patients (for example, applying clinical prediction rules using signs, symptoms, EWS thresholds) to avoid serious illness?
3.	Objective	To assess the value and usefulness of, and clinical decision rules based on, different symptoms, signs and EWS (individually or in combination) for guiding management in patients with suspected ARI. Any relevant economic evaluations identified will be summarised as appropriate.
4.	Searches	A search strategy has been developed in Ovid MEDLINE to identify systematic reviews of relevance to the initial assessment of suspected ARI, focusing on signs or symptoms and EWS. The search is structured as follows: Respiratory tract infections, adapted from terms shared by the Bristol team AND Assessment of signs/symptoms, triage, early warning scores or clinical decision rules AND

		Systematic reviews, adapted from a previous strategy shared by NICE The strategy will be translated, as appropriate for use in the other databases. The following databases will be searched: • Cochrane Database of Systematic Reviews (CDSR) via Wiley • MEDLINE ALL via Ovid • Embase via Ovid Database functionality will be used, where available, to exclude: • Animal studies • Editorials, letters, news items and commentaries • Conference abstracts and posters • Registry entries for ongoing clinical trials • Theses and dissertations • Papers not published in the English language. No date limits will be applied. Standard NICE filters will be used to limit results to systematic reviews. Other sources: • The reference lists of potentially relevant references will be checked. Separate searches to identify economic evaluations relevant to the initial assessment of suspected ARI will be undertaken. The search strategy will be structured as follows: Respiratory tract infections, adapted from terms shared by the Bristol team AND Assessment of signs/symptoms, triage, early warning systems or clinical decision rules AND

		Economic evaluations, using a filter developed for populating the NHS Economic Evaluations Database The following databases will be searched: MEDLINE (Ovid), Embase (Ovid), EconLit (Ovid) and the archive of the NHS Economic Evaluations Database (NHS EED). Further targeted searches for primary studies will be carried out if necessary, depending on any gaps in the evidence found after searching and screening for systematic reviews. The full search strategies for all databases will be published in the final review.
5.	Condition or domain being studied	Suspected ARI.
6.	Population	Inclusion: People aged 16 years or over with suspected ARI (including: bronchitis, common cold, glandular fever, influenza, laryngitis, sore throat (pharyngitis and tonsillitis), pneumonia and severe acute respiratory syndrome (SARS)). Exclusion: People aged 16 or over: • With a confirmed COVID-19 diagnosis. • Who are hospital in-patients (including those with hospital acquired respiratory infections). • Who have a respiratory infection during end-of-life care. • With aspiration pneumonia, bronchiectasis, cystic fibrosis (CF), or known immunosuppression. Children and young people under 16 years.
7.	Phenomenon of interest	Symptoms, signs, and externally validated EWS for the assessment of suspected ARI, including: Cough, coughing up blood, purulent sputum, malaise, coryza, temperature/signs of fever, sore throat, hoarse voice, breathlessness and/or increased respiratory rate, wheeze/chest tightness, cyanosis, loss of appetite, lethargy, agitation, confusion, delirium, drowsiness, headache, rigors, chest pain, monitoring parameters based on digital technologies where available (e.g. pulse oximetry, peak flow), sudden deterioration in any of the above, EWS (including NEWS/NEWS2, CRB65/CURB65, CENTOR criteria), and any combination of the above.

8.	Setting	Inclusion: • Remote settings (via telephone, video call, online app, e-mail, or text message, e.g., NHS 111, 999 call centres or calls from GP practices) • Face-to-face settings (e.g., the person's home, a care home, primary care [including community pharmacy or ARI hubs], NHS walk-in centres, emergency departments). Exclusion: Hospital in-patient settings.
9.	Types of study to be included	Systematic reviews; no restrictions will be made based on the study designs included in the systematic reviews or on review date (as it is unlikely that symptoms and signs of suspected ARI have changed significantly over time). Systematic reviews will be identified by the use of all of the following: • clear and unambiguous eligibility criteria • comprehensive search (either stated as their aim or implied by use of 2 or more bibliographic databases) • details of included studies separately identifiable (for example with a table of characteristics, and references for all included studies) If insufficient systematic reviews are identified, primary studies will be eligible for inclusion. Prospective cohorts are the preferred cohort study type, but if these do not provide adequate data to make a decision, retrospective cohorts will be considered. In some cases, comparative studies, including RCTs, may be relevant. Full economic evaluations comparing two or more alternatives in terms of both costs and consequences (i.e., cost-minimisation, cost-effectiveness, cost-utility and cost-benefit analyses).
10.	Other exclusion criteria	• Studies not published in English • Pre-prints • Dissertations and theses • Animal studies

		• Conference abstracts and posters • Derivation studies
11.	Context	For people over 16 years with suspected ARI, initial consultations with the health system may occur remotely (for example, through online apps, email exchange or text message, via telephone through NHS 111 or with a GP, via video call, or direct to 999 emergency call centres) or face-to-face (for example, in the person's home or care home, in primary care including community pharmacy or ARI hubs, in NHS walk-in centres, and in emergency departments). Those with suspected respiratory infections can be advised to remain at home for self-monitoring (with or without being prescribed antibiotics or antivirals), referred to ARI virtual wards for further monitoring, or referred to, and/or admitted to, a hospital. ARIs cover a wide range of different conditions. The primary concerns here are conditions for which signs, symptoms and EWS, either individually or in combination, may be used to identify serious cases or predict potential to deteriorate (which would require a different level of monitoring and healthcare). This review aims to assess the evidence for using signs, symptoms and EWS to guide clinical decision-making and triage decisions for people with ARI.

12.	Primary outcomes (critical outcomes)	Assessed within 4 weeks of consultation:
		• Hospital admission
		• Escalation of care to any setting including:
		  ○ Face to face consultation
		  ○ Re-consultation/appointment
		  ○ Virtual ward
		  ○ Referral to ARI hub
		  ○ A&E visit
		  ○ Unplanned hospital admission
		• Hospital length of stay
		• Follow-up consultation/ongoing monitoring
		• Antibiotic/antiviral use
		• Time to clinical cure/resolution of symptoms

		• Mortality (The 4 week time period was chosen to ensure outcomes relevant solely to the assessment of signs, symptoms and EWS are identified. During this time period, it is anticipated that additional follow-up tests are likely to have been considered and/or undertaken based on patient symptoms (for example CRP and rapid PCR tests) and such tests are being covered in RQ1.3, Warwick ESG)
13.	Secondary outcomes (important outcomes)	• Patient acceptability • Patient preference • HRQoL (using a validated scale) (We will report whatever measure is included in the reviews (such outcomes are often recorded qualitatively particularly in patient acceptability, but formal questionnaires can be used, for example, the Patient Satisfaction Questionnaire (PSQ) and the Client Satisfaction Questionnaire (CSQ))
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 assessed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. This review will make use of the priority screening functionality within the EPPI-Reviewer software. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see *Developing NICE guidelines: the manual section 6.2*).
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using appropriate checklists as described in *Developing NICE guidelines: the manual*. Included systematic reviews will be assessed using the Risk of Bias in Systematic Reviews tool (ROBIS).[11] Quality assessment will be undertaken by one reviewer and checked by a second reviewer.
16.	Strategy for data synthesis	Systematic reviews will be combined in a narrative synthesis, taking account of any studies common to more than one review. We will report the GRADE assessments presented in systematic reviews but if this is not reported then we will assess the certainty of the evidence by using data reported in systematic reviews where possible. Given the very short timescale for this project, a pragmatic approach is necessitated.

		Key characteristics including participants, setting, intervention, comparators (where applicable), results, and review quality will be tabulated and described. This will provide a clear descriptive summary of the studies, assessing the strength of the evidence and the consistency of the findings. Differences between studies will be explored along with possible explanations for any observed inconsistencies. If no eligible systematic reviews are identified, where available, relevant primary studies will be included. Where eligible primary studies are identified and sufficient clinically and statistically homogenous data are available, data may be pooled using appropriate meta-analytic techniques. Given the very short timescale for this project, a pragmatic approach is necessitated; we will provide a protocol amendment for any additional data synthesis of primary studies, detailing what will be achievable in the time remaining. The quality of the economic evaluations will be assessed using an appropriate checklist. Information will be tabulated and summarised.	
17.	Analysis of sub-groups	Where possible, separate narrative summaries of evidence will be presented for the following subgroups: • Consultation setting • Age of patient (65 years and under, 66 – 80 years, over 80 years) • Presence of chronic co-morbidity (for example, COPD) • Pregnancy & post-partum (up to 28 days)	
18.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☒	Epidemiologic
		☒	Service Delivery
		☐	Other (please specify)

19.	Language	English
20.	Country	England
24.	Named contact	Rachel Churchill **e-mail** Rachel.Churchill@york.ac.uk **Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and NIHR
25.	Review team members	York ESG: Ros Wade – Reviewer Chinyereugo Umemneku-Chikere - Reviewer Melissa Harden – Information Specialist Rachel Churchill – ESG Senior Lead Alison Eastwood – ESG Senior Lead Kerry Dwan – Senior statistics advisor Jasmine Deng – Health economic reviewer Rob Hodgson – Health economics advisor
26.	Funding sources/sponsor	NIHR
27.	Conflicts of interest	None

1

Appendix B – Literature search strategies

Search strategies to identify clinical reviews

Review questions

In people aged 16 years or over with suspected acute respiratory infection (ARI):

1. What are the signs, symptoms and early warning scores (EWS) that have been evaluated?

2. What are the strategies for the triage of patients (for example, applying clinical prediction rules using signs, symptoms, EWS thresholds) to avoid serious illness?

MEDLINE ALL

via Ovid http://ovidsp.ovid.com/

Date range: 1946 to May 11, 2023

Date searched: 15th May 2023

Records retrieved: 2659

1 exp Respiratory Tract Infections/ (605237)

2 ((airway$ or bronchopulmonar$ or broncho-pulmonar$ or tracheobronch$ or tracheo-bronch$ or pulmonar$ tract or pulmonary or respirat$ tract or respiratory or chest or lung? or lobar or pleura?) adj3 (infect$ or coinfect$ or inflam$ or swollen or swelling$ or abscess$)).ti,ab. (153445)

3 (bronchit$ or bronchiolit$ or allergic bronchopulmon$ or bronchopneumon$ or common cold$ or coryza or croup or empyem$ or epipharyngit$ or epiglottit$ or epiglotit$ or flu or influenza or laryngit$ or laryngotracheobronchit$ or laryngo tracheo bronchit$ or laryngo tracheobronchit$ or laryngotracheit$ or nasopharyngit$ or otitis media or parainfluenza or pharyngit$ or pleurisy or pneumoni$ or pleuropneumoni$ or rhinit$ or rhinopharyngit$ or rhinosinusit$ or severe acute respiratory syndrome or SARS or sinusit$ or sore throat$ or throat infection$ or supraglottit$ or supraglotit$ or tonsillit$ or tonsilit$ or tracheit$ or whooping cough or pertussis or pertusis).mp. (821333)

4 (ARTI or RTI or LRTI or URTI or ALRI or AURI or SARI).ti,ab. (7276)

5 Infectious Mononucleosis/ (7318)

6 (glandular fever or Infectious Mononucleosis or Epstein-Barr).ti,ab. (40792)

7 ((strep$ adj3 (throat$ or pharyn$ or tonsil$)) or (strep$ and (airway$ or pulmonary or brochopulmonar$ or brocho-pulmonar$ or respiratory$))).mp. (22155)

8 ((acute$ or exacerbat$ or flare$) adj3 (copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway$ disease or chronic obstructive lung disease)).mp. (10290)

9 ((acute$ or subacute$ or exacerbat$ or prolonged) adj3 cough$).mp. (1546)

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (1131600)

11 early warning score/ (380)

12 "Severity of Illness Index"/ (270315)

13 (early warning$ or red flag$ or (flag$ adj2 early)).ti,ab. (12990)

14 (severity adj3 (score$ or scoring or scale$ or tool$ or instrument$ or index$ or indice$ or calculat$ or algorithm$ or metric$ or measur$ or criteri$ or code$)).ti,ab. (79034)

15 (severity adj3 (assess$ or estimat$ or evaluat$ or classif$ or rate? or rating? or value? or quantif$ or grade$ or chart$ or equation$ or table$ or model$ or framework$ or predict$)).ti,ab. (70990)

16 11 or 12 or 13 or 14 or 15 (386863)

17 (curb65 or crb65 or curb-65 or crb-65 or news2 or enews or pnews).ti,ab. (1132)

18 ((curb or news) adj3 (criteri$ or rule$ or scor$ or predict$ or tool$)).ti,ab. (1172)

19 CENTOR.ti,ab. (135)

20 (PMEWS or eMEWS).ti,ab. (20)

21 (McIsaac adj (score$ or scoring or criteri$)).ti,ab. (37)

22 (sino-nasal outcome test$ or SNOT-22 or SNOT22).ti,ab. (1372)

23 (pneumonia severity index or PSI or (PORT adj (Score$ or scoring))).ti,ab. (20696)

24 17 or 18 or 19 or 20 or 21 or 22 or 23 (23631)

25 16 or 24 (408300)

26 10 and 25 (30022)

27 Triage/ (14830)

28 (triage$ or triaging).ti,ab. (27182)

29 ((stratif$ or priorit$ or classif$) adj3 (patient$ or outpatient$)).ti,ab. (110619)

30 ((stratif$ or priorit$ or classif$) adj3 (symptom$ or sign? or illness$ or disease$ or disorder$ or severity or risk$)).ti,ab. (122512)

31 27 or 28 or 29 or 30 (243129)

32 10 and 31 (14211)

33 Symptom Assessment/ (7065)

34 Patient Acuity/ (2591)

35 ((initial or first or primary or point of care) adj3 (assess$ or evaluat$ or examin$ or screen$) adj3 (patient$ or outpatient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (13243)

36 ((sign? or symptom$) adj2 (score$ or scoring)).ti,ab. (31415)

37 ((assess$ or evaluat$ or determin$ or detect$ or analys$ or screen$) adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (28501)

38 ((patient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$) adj3 acuity).ti,ab. (7682)

39 33 or 34 or 35 or 36 or 37 or 38 (88339)

40 10 and 39 (10530)

41 Clinical Decision Rules/ (911)

42 (clinical$ adj5 (decision$ or predicti$) adj5 (aid? or algorithm? or characteristic? or criteri$ or evaluation? or index or indices or marker? or method$ or model$ or panel? or parameter? or rule or rules or score? or scoring or screen$ or signs or symptoms or system? or technique? or test$ or tool? or value? or variable$)).mp. (44013)

43 (clinical$ adj (predicti$ or predictor$)).ti,ab. (11212)

44 (rule in or ruled in or rule out or ruled out).ti,ab. (60226)

45 (predict$ adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (9210)

46 ((predict$ or prognos$ or cluster$) adj3 (sign? or symptom$)).ti,ab. (28230)

47 41 or 42 or 43 or 44 or 45 or 46 (145502)

48 10 and 47 (8781)

49 26 or 32 or 40 or 48 (55802)

50 "systematic review".pt. (228202)

51 meta analysis.pt. (180733)

52 (meta analy$ or metanaly$ or metaanaly$).ti,ab. (268778)

53 ((systematic$ or evidence$) adj3 (review$ or overview$)).ti,ab. (359433)

54 (reference list$ or bibliograph$ or hand search$ or manual search$ or relevant journals).ab. (54013)

55 (search strategy or search criteria or systematic search or study selection or data extraction).ab. (80940)

56 (search$ adj4 literature).ab. (96383)

57 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. (356783)

58 cochrane.jw. (16330)

59 ((diagnos$ or prognos$) adj2 review$).ti,ab. (11734)

60 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 59 (686228)

61 49 and 60 (2766)

62 exp animals/ not humans.sh. (5120552)

63 61 not 62 (2761)

64 limit 63 to english language (2704)

65 (comment or editorial or letter or news).pt. (2359631)

66 64 not 65 (2659)

Key:

/ = subject heading (MeSH heading)

sh = subject heading (MeSH heading)

exp = exploded subject heading (MeSH heading)

$ = truncation

? = optional wildcard – one or no characters

ti,ab = terms in title or abstract fields

mp = multi-purpose field search – terms in title, original title, abstract, name of substance word, or subject heading word

pt = publication type

jw = journal word

adj3 = terms within three words of each other (any order)

adj = terms next to each other in order specified

Embase

via Ovid http://ovidsp.ovid.com/

Date range: 1974 to 2023 May 12

Date searched: 15th May 2023

Records retrieved: 2632

1 exp respiratory tract infection/ (486791)

2 ((airway$ or bronchopulmonar$ or broncho-pulmonar$ or tracheobronch$ or tracheo-bronch$ or pulmonar$ tract or pulmonary or respirat$ tract or respiratory or chest or lung? or

lobar or pleura?) adj3 (infect$ or coinfect$ or inflam$ or swollen or swelling$ or abscess$)).ti,ab. (227122)

3 (bronchit$ or bronchiolit$ or allergic bronchopulmon$ or bronchopneumon$ or common cold$ or coryza or croup or empyem$ or epipharyngit$ or epiglottit$ or epiglotit$ or flu or influenza or laryngit$ or laryngotracheobronchit$ or laryngo tracheo bronchit$ or laryngo tracheobronchit$ or laryngotracheit$ or nasopharyngit$ or otitis media or parainfluenza or pharyngit$ or pleurisy or pneumoni$ or pleuropneumoni$ or rhinit$ or rhinopharyngit$ or rhinosinusit$ or severe acute respiratory syndrome or SARS or sinusit$ or sore throat$ or throat infection$ or supraglottit$ or supraglotit$ or tonsillit$ or tonsilit$ or tracheit$ or whooping cough or pertussis or pertusis).mp. (1187643)

4 (ARTI or RTI or LRTI or URTI or ALRI or AURI or SARI).ti,ab. (11236)

5 mononucleosis/ (2883)

6 (glandular fever or infectious mononucleosis or Epstein-Barr).ti,ab. (47931)

7 streptococcal pharyngitis/ (1777)

8 ((strep$ adj3 (throat$ or pharyn$ or tonsil$)) or (strep$ and (airway$ or pulmonary or brochopulmonar$ or brocho-pulmonar$ or respiratory$))).mp. (42535)

9 ((acute$ or exacerbat$ or flare$) adj3 (copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway$ disease or chronic obstructive lung disease)).mp. (19296)

10 ((acute$ or subacute$ or exacerbat$ or prolonged) adj3 cough$).mp. (2474)

11 or/1-10 (1509554)

12 exp early warning score/ (1794)

13 disease severity assessment/ (9886)

14 "severity of illness index"/ (20395)

15 (early warning$ or red flag$ or (flag$ adj2 early)).ti,ab. (17967)

16 (severity adj3 (score$ or scoring or scale$ or tool$ or instrument$ or index$ or indice$ or calculat$ or algorithm$ or metric$ or measur$ or criteri$ or code$)).ti,ab. (129233)

17 (severity adj3 (assess$ or estimat$ or evaluat$ or classif$ or rate? or rating? or value? or quantif$ or grade$ or chart$ or equation$ or table$ or model$ or framework$ or predict$)).ti,ab. (115235)

18 12 or 13 or 14 or 15 or 16 or 17 (261868)

19 (curb65 or crb65 or curb-65 or crb-65 or news2 or enews or pnews).ti,ab. (2054)

20 ((curb or news) adj3 (criteri$ or rule$ or scor$ or predict$ or tool$)).ti,ab. (1970)

21 CENTOR.ti,ab. (185)

22 (PMEWS or eMEWS).ti,ab. (26)

23 (McIsaac adj (score$ or scoring or criteri$)).ti,ab. (49)

24 (sino-nasal outcome test$ or SNOT-22 or SNOT22).ti,ab. (2010)

25 (pneumonia severity index or PSI or (PORT adj (score$ or scoring))).ti,ab. (21566)

26 19 or 20 or 21 or 22 or 23 or 24 or 25 (26187)

27 18 or 26 (284907)

28 11 and 27 (24815)

29 patient triage/ (3244)

30 (triage$ or triaging).ti,ab. (43825)

31 ((stratif$ or priorit$ or classif$) adj3 (patient$ or outpatient$)).ti,ab. (201540)

32 ((stratif$ or priorit$ or classif$) adj3 (symptom$ or sign? or illness$ or disease$ or disorder$ or severity or risk$)).ti,ab. (202687)

33 29 or 30 or 31 or 32 (406394)

34 11 and 33 (22210)

35 symptom assessment/ (11857)

36 patient acuity/ (1293)

37 ((initial or first or primary or point of care) adj3 (assess$ or evaluat$ or examin$ or screen$) adj3 (patient$ or outpatient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (22489)

38 ((sign? or symptom$) adj2 (score$ or scoring)).ti,ab. (51668)

39 ((assess$ or evaluat$ or determin$ or detect$ or analys$ or screen$) adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (46809)

40 ((patient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$) adj3 acuity).ti,ab. (11416)

41 35 or 36 or 37 or 38 or 39 or 40 (140927)

42 11 and 41 (15434)

43 clinical decision rule/ (684)

44 (clinical$ adj5 (decision$ or predicti$) adj5 (aid? or algorithm? or characteristic? or criteri$ or evaluation? or index or indices or marker? or method$ or model$ or panel? or parameter? or rule or rules or score? or scoring or screen$ or signs or symptoms or system? or technique? or test$ or tool? or value? or variable$)).mp. (62551)

45 (clinical$ adj (predicti$ or predictor$)).ti,ab. (18367)

46 (rule in or ruled in or rule out or ruled out).ti,ab. (93769)

47 (predict$ adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (14169)

48 ((predict$ or prognos$ or cluster$) adj3 (sign? or symptom$)).ti,ab. (39509)

49 43 or 44 or 45 or 46 or 47 or 48 (217048)

50 11 and 49 (15032)

51 28 or 34 or 42 or 50 (68399)

52 "systematic review"/ (434122)

53 exp meta analysis/ (293135)

54 (meta analy$ or metanaly$ or metaanaly$).ti,ab. (356347)

55 ((systematic or evidence) adj2 (review$ or overview$)).ti,ab. (412624)

56 (reference list$ or bibliograph$ or hand search$ or manual search$ or relevant journals).ab. (67522)

57 (search strategy or search criteria or systematic search or study selection or data extraction).ab. (100509)

58 (search$ adj4 literature).ab. (125065)

59 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. (451666)

60 ((pool$ or combined) adj2 (data or trials or studies or results)).ab. (92673)

61 cochrane.jw. (24683)

62 ((diagnos$ or prognos$) adj2 review$).ti,ab. (17027)

63 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 (980485)

64 51 and 63 (3452)

65 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (6800393)

66 64 not 65 (3426)

67 (editorial or letter or note).pt. (3015508)

68 66 not 67 (3396)

69 (conference abstract$ or conference review or conference paper or conference proceeding).db,pt,su. (5535870)

70 68 not 69 (2716)

71 preprint.pt. (65307)

72 70 not 71 (2694)

73 limit 72 to english language (2632)

Key:

/ = subject heading (Emtree heading)

exp = exploded subject heading (Emtree heading)

$ = truncation

? = optional wildcard – one or no characters

ti,ab = terms in title or abstract fields

mp = multi-purpose field search – terms in title, original title, abstract, name of substance word, or subject heading word

pt = publication type

jw = journal word

db = database

su = source type

adj3 = terms within three words of each other (any order)

adj = terms next to each other in order specified

Cochrane Database of Systematic Reviews (CDSR)

via Wiley http://onlinelibrary.wiley.com/

Issue: Issue 5 of 12, May 2023

Date searched: 15th May 2023

Records retrieved: 203

#1 MeSH descriptor: [Respiratory Tract Infections] explode all trees 23846

#2 ((airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonar* tract or pulmonary or (respirat*next tract) or respiratory or chest or lung? or lobar or pleura?) near/3 (infect* or coinfect* or inflam* or swollen or swelling* or abscess*)):ti,ab,kw 30789

#3 (bronchit* or bronchiolit* or (allergic next bronchopulmon*) or bronchopneumon* or (common next cold*) or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or (laryngo next trachea next bronchit*) or (laryngo next tracheobronchit*) or laryngotracheit* or nasopharyngit* or “otitis media” or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or “severe acute respiratory syndrome” or SARS or sinusit* or (sore next throat*) or (throat next infection*) or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or “whooping cough” or pertussis or pertusis):ti,ab,kw 69533

#4 MeSH descriptor: [Otitis Media] explode all trees 1392

#5 (ARTI or RTI or LRTI or URTI or ALRI or AURI or SARI):ti,ab,kw 1608

#6 MeSH descriptor: [Infectious Mononucleosis] this term only 62

#7 ("glandular fever" or "Infectious Mononucleosis" or Epstein-Barr):ti,ab,kw 599

#8 ((strep* near/3 (throat* or pharyn* or tonsil*)) or (strep* and (airway* or pulmonary or brochopulmonar* or brocho-pulmonar* or respiratory*))):ti,ab,kw 1729

#9 ((acute* or exacerbat* or flare*) near/3 (copd or coad or "chronic obstructive pulmonary disease" or ("chronic obstructive" next airway* next disease) or "chronic obstructive lung disease")):ti,ab,kw 4040

#10 ((acute* or subacute* or exacerbat* or prolonged) near/3 cough*):ti,ab,kw 525

#11 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 97500

#12 MeSH descriptor: [Early Warning Score] this term only 11

#13 MeSH descriptor: [Severity of Illness Index] this term only 22685

#14 ((early next warning*) or (red next flag*) or (flag* near/2 early)):ti,ab,kw 675

#15 (severity near/3 (score* or scoring or scale* or tool* or instrument* or index* or indice* or calculat* or algorithm* or metric* or measur* or criteri* or code*)):ti,ab,kw 47560

#16 (severity near/3 (assess* or estimat* or evaluat* or classif* or rate? or rating? or value? or quantif* or grade* or chart* or equation* or table* or model* or framework* or predict*)):ti,ab,kw 15000

#17 #12 or #13 or #14 or #15 or #16 57740

#18 (curb65 or crb65 or curb-65 or crb-65 or news2 or enews or pnews):ti,ab,kw 163

#19 ((curb or news) near/3 (criteri* or rule* or scor* or predict* or tool*)):ti,ab,kw 196

#20 CENTOR:ti,ab,kw 33

#21 (PMEWS or eMEWS):ti,ab,kw 2

#22 (McIsaac next (score* or scoring or criteri*)):ti,ab,kw 5

#23 (("sino-nasal outcome" next test*) or SNOT-22 or SNOT22):ti,ab,kw 630

#24 ("pneumonia severity index" or PSI or (PORT next (score* or scoring))):ti,ab,kw 1055

#25 #18 or #19 or #20 or #21 or #22 or #23 or #24 1995

#26 #17 or #25 59302

#27 #11 and #26 in Cochrane Reviews, Cochrane Protocols 50

#28 MeSH descriptor: [Triage] this term only 400

#29 (triage* or triaging):ti,ab,kw 2255

#30 ((stratif* or priorit* or classif*) near/3 (patient* or outpatient*)):ti,ab,kw 21550

#31 ((stratif* or priorit* or classif*) near/3 (symptom* or sign? or illness* or disease* or disorder* or severity or risk*)):ti,ab,kw 16858

#32 #28 or #29 or #30 or #31 38181

#33 #11 and #32 in Cochrane Reviews, Cochrane Protocols 22

#34 MeSH descriptor: [Symptom Assessment] this term only 502

#35 MeSH descriptor: [Patient Acuity] this term only 182

#36 ((initial or first or primary or point of care) near/3 (assess* or evaluat* or examin* or screen*) near/3 (patient* or outpatient* or sign? or symptom* or illness* or disease* or disorder* or infection*)):ti,ab,kw 57714

#37 ((sign? or symptom*) near/2 (score* or scoring)):ti,ab,kw 18921

#38 ((assess* or evaluat* or determin* or detect* or analys* or screen*) near/5 (severe* or severity or serious*) near/5 (sign? or symptom* or illness* or disease* or disorder* or infection*)):ti,ab,kw 7534

#39 ((patient* or sign? or symptom* or illness* or disease* or disorder* or infection*) near/3 acuity):ti,ab,kw 1326

#40 #34 or #35 or #36 or #37 or #38 or #39 81543

#41 #11 and #40 in Cochrane Reviews, Cochrane Protocols 130

#42 MeSH descriptor: [Clinical Decision Rules] this term only 43

#43 (clinical* near/5 (decision* or predicti*) near/5 (aid? or algorithm? or characteristic? or criteri* or evaluation? or index or indices or marker? or method* or model* or panel? or parameter? or rule or rules or score? or scoring or screen* or signs or symptoms or system? or technique? or test* or tool? or value? or variable*)):ti,ab,kw 5920

#44 (clinical* next (predicti* or predictor*)):ti,ab,kw 984

#45 (rule in or ruled in or rule out or ruled out):ti,ab,kw 5641

#46 (predict* near/5 (severe* or severity or serious*) near/5 (sign? or symptom* or illness* or disease* or disorder* or infection*)):ti,ab,kw 599

#47 ((predict* or prognos* or cluster*) near/3 (sign? or symptom*)):ti,ab,kw 2592

#48 #42 or #43 or #44 or #45 or #46 or #47 14792

#49 #11 and #48 in Cochrane Reviews, Cochrane Protocols 43

#50 #27 or #33 or #41 or #49 in Cochrane Reviews, Cochrane Protocols 203

Key:

MeSH descriptor = subject heading (MeSH heading)

* = truncation

? = wildcard - zero or one characters

ti,ab,kw = terms in title, abstract or keyword fields

near/3 = terms within three words of each other (any order)

next = terms are next to each other

Search strategies to identify economic studies

Ovid MEDLINE(R) ALL

via Ovid http://ovidsp.ovid.com/

Date range searched: <1946 to May 11, 2023>

Date searched: 15th May 2023

Records retrieved: 1778

1 exp Respiratory Tract Infections/ (605237)

2 ((airway$ or bronchopulmonar$ or broncho-pulmonar$ or tracheobronch$ or tracheo-bronch$ or pulmonar$ tract or pulmonary or respirat$ tract or respiratory or chest or lung? or lobar or pleura?) adj3 (infect$ or coinfect$ or inflam$ or swollen or swelling$ or abscess$)).ti,ab. (153445)

3 (bronchit$ or bronchiolit$ or allergic bronchopulmon$ or bronchopneumon$ or common cold$ or coryza or croup or empyem$ or epipharyngit$ or epiglottit$ or epiglotit$ or flu or influenza or laryngit$ or laryngotracheobronchit$ or laryngo tracheo bronchit$ or laryngo tracheobronchit$ or laryngotracheit$ or nasopharyngit$ or otitis media or parainfluenza or pharyngit$ or pleurisy or pneumoni$ or pleuropneumoni$ or rhinit$ or rhinopharyngit$ or rhinosinusit$ or severe acute respiratory syndrome or SARS or sinusit$ or sore throat$ or throat infection$ or supraglottit$ or supraglotit$ or tonsillit$ or tonsilit$ or tracheit$ or whooping cough or pertussis or pertusis).mp. (821333)

4 (ARTI or RTI or LRTI or URTI or ALRI or AURI or SARI).ti,ab. (7276)

5 Infectious Mononucleosis/ (7318)

6 (glandular fever or Infectious Mononucleosis or Epstein-Barr).ti,ab. (40792)

7 ((strep$ adj3 (throat$ or pharyn$ or tonsil$)) or (strep$ and (airway$ or pulmonary or brochopulmonar$ or brocho-pulmonar$ or respiratory$))).mp. (22155)

8 ((acute$ or exacerbat$ or flare$) adj3 (copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway$ disease or chronic obstructive lung disease)).mp. (10290)

9 ((acute$ or subacute$ or exacerbat$ or prolonged) adj3 cough$).mp. (1546)

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (1131600)

11 early warning score/ (380)

12 "Severity of Illness Index"/ (270315)

13 (early warning$ or red flag$ or (flag$ adj2 early)).ti,ab. (12990)

14 (severity adj3 (score$ or scoring or scale$ or tool$ or instrument$ or index$ or indice$ or calculat$ or algorithm$ or metric$ or measur$ or criteri$ or code$)).ti,ab. (79034)

15 (severity adj3 (assess$ or estimat$ or evaluat$ or classif$ or rate? or rating? or value? or quantif$ or grade$ or chart$ or equation$ or table$ or model$ or framework$ or predict$)).ti,ab. (70990)

16 11 or 12 or 13 or 14 or 15 (386863)

17 (curb65 or crb65 or curb-65 or crb-65 or news2 or enews or pnews).ti,ab. (1132)

18 ((curb or news) adj3 (criteri$ or rule$ or scor$ or predict$ or tool$)).ti,ab. (1172)

19 CENTOR.ti,ab. (135)

20 (PMEWS or eMEWS).ti,ab. (20)

21 (McIsaac adj (score$ or scoring or criteri$)).ti,ab. (37)

22 (sino-nasal outcome test$ or SNOT-22 or SNOT22).ti,ab. (1372)

23 (pneumonia severity index or PSI or (PORT adj (Score$ or scoring))).ti,ab. (20696)

24 17 or 18 or 19 or 20 or 21 or 22 or 23 (23631)

25 16 or 24 (408300)

26 10 and 25 (30022)

27 Triage/ (14830)

28 (triage$ or triaging).ti,ab. (27182)

29 ((stratif$ or priorit$ or classif$) adj3 (patient$ or outpatient$)).ti,ab. (110619)

30 ((stratif$ or priorit$ or classif$) adj3 (symptom$ or sign? or illness$ or disease$ or disorder$ or severity or risk$)).ti,ab. (122512)

31 27 or 28 or 29 or 30 (243129)

32 10 and 31 (14211)

33 Symptom Assessment/ (7065)

34 Patient Acuity/ (2591)

35 ((initial or first or primary or point of care) adj3 (assess$ or evaluat$ or examin$ or screen$) adj3 (patient$ or outpatient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (13243)

36 ((sign? or symptom$) adj2 (score$ or scoring)).ti,ab. (31415)

37 ((assess$ or evaluat$ or determin$ or detect$ or analys$ or screen$) adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (28501)

38 ((patient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$) adj3 acuity).ti,ab. (7682)

39 33 or 34 or 35 or 36 or 37 or 38 (88339)

40 10 and 39 (10530)

41 Clinical Decision Rules/ (911)

42 (clinical$ adj5 (decision$ or predicti$) adj5 (aid? or algorithm? or characteristic? or criteri$ or evaluation? or index or indices or marker? or method$ or model$ or panel? or parameter? or rule or rules or score? or scoring or screen$ or signs or symptoms or system? or technique? or test$ or tool? or value? or variable$)).mp. (44013)

43 (clinical$ adj (predicti$ or predictor$)).ti,ab. (11212)

44 (rule in or ruled in or rule out or ruled out).ti,ab. (60226)

45 (predict$ adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (9210)

46 ((predict$ or prognos$ or cluster$) adj3 (sign? or symptom$)).ti,ab. (28230)

47 41 or 42 or 43 or 44 or 45 or 46 (145502)

48 10 and 47 (8781)

49 26 or 32 or 40 or 48 (55802)

50 Economics/ (27500)

51 exp "costs and cost analysis"/ (264277)

52 Economics, Dental/ (1921)

53 exp economics, hospital/ (25710)

54 Economics, Medical/ (9245)

55 Economics, Nursing/ (4013)

56 Economics, Pharmaceutical/ (3103)

57 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (1030924)

58 (expenditure$ not energy).ti,ab. (36561)

59 value for money.ti,ab. (2105)

60 budget$.ti,ab. (35216)

61 or/50-60 (1195231)

62 ((energy or oxygen) adj cost).ti,ab. (4741)

63 (metabolic adj cost).ti,ab. (1698)

64 ((energy or oxygen) adj expenditure).ti,ab. (28877)

65 or/62-64 (34259)

66 61 not 65 (1187317)

67 49 and 66 (2910)

68 exp animals/ not humans/ (5120552)

69 67 not 68 (2866)

70 limit 69 to english language (2727)

71 (comment or editorial or letter or news).pt. (2359631)

72 70 not 71 (2699)

73 limit 72 to yr="2014 -Current" (1783)

74 remove duplicates from 73 (1778)

Key:

/ = indexing term (Medical Subject Heading: MeSH)

exp = exploded indexing term (MeSH)

$ = truncation

ti,ab = terms in either title or abstract fields

mp = multipurpose

? = wildcard for one additional letter

adj2 = terms within two words of each other (any order)

Embase

via Ovid http://ovidsp.ovid.com/

Date range searched: <1974 to 2023 May 12>

Date searched: 15th May 2023

Records retrieved: 1705

1 exp respiratory tract infection/ (486791)

2 ((airway$ or bronchopulmonar$ or broncho-pulmonar$ or tracheobronch$ or tracheo-bronch$ or pulmonar$ tract or pulmonary or respirat$ tract or respiratory or chest or lung? or lobar or pleura?) adj3 (infect$ or coinfect$ or inflam$ or swollen or swelling$ or abscess$)).ti,ab. (227122)

3 (bronchit$ or bronchiolit$ or allergic bronchopulmon$ or bronchopneumon$ or common cold$ or coryza or croup or empyem$ or epipharyngit$ or epiglottit$ or epiglotit$ or flu or influenza or laryngit$ or laryngotracheobronchit$ or laryngo tracheo bronchit$ or laryngo tracheobronchit$ or laryngotracheit$ or nasopharyngit$ or otitis media or parainfluenza or pharyngit$ or pleurisy or pneumoni$ or pleuropneumoni$ or rhinit$ or rhinopharyngit$ or rhinosinusit$ or severe acute respiratory syndrome or SARS or sinusit$ or sore throat$ or throat infection$ or supraglottit$ or supraglotit$ or tonsillit$ or tonsilit$ or tracheit$ or whooping cough or pertussis or pertusis).mp. (1187643)

4 (ARTI or RTI or LRTI or URTI or ALRI or AURI or SARI).ti,ab. (11236)

5 mononucleosis/ (2883)

6 (glandular fever or infectious mononucleosis or Epstein-Barr).ti,ab. (47931)

7 streptococcal pharyngitis/ (1777)

8 ((strep$ adj3 (throat$ or pharyn$ or tonsil$)) or (strep$ and (airway$ or pulmonary or brochopulmonar$ or brocho-pulmonar$ or respiratory$))).mp. (42535)

9 ((acute$ or exacerbat$ or flare$) adj3 (copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway$ disease or chronic obstructive lung disease)).mp. (19296)

10 ((acute$ or subacute$ or exacerbat$ or prolonged) adj3 cough$).mp. (2474)

11 or/1-10 (1509554)

12 exp early warning score/ (1794)

13 disease severity assessment/ (9886)

14 "severity of illness index"/ (20395)

15 (early warning$ or red flag$ or (flag$ adj2 early)).ti,ab. (17967)

16 (severity adj3 (score$ or scoring or scale$ or tool$ or instrument$ or index$ or indice$ or calculat$ or algorithm$ or metric$ or measur$ or criteri$ or code$)).ti,ab. (129233)

17 (severity adj3 (assess$ or estimat$ or evaluat$ or classif$ or rate? or rating? or value? or quantif$ or grade$ or chart$ or equation$ or table$ or model$ or framework$ or predict$)).ti,ab. (115235)

18 12 or 13 or 14 or 15 or 16 or 17 (261868)

19 (curb65 or crb65 or curb-65 or crb-65 or news2 or enews or pnews).ti,ab. (2054)

20 ((curb or news) adj3 (criteri$ or rule$ or scor$ or predict$ or tool$)).ti,ab. (1970)

21 CENTOR.ti,ab. (185)

22 (PMEWS or eMEWS).ti,ab. (26)

23 (McIsaac adj (score$ or scoring or criteri$)).ti,ab. (49)

24 (sino-nasal outcome test$ or SNOT-22 or SNOT22).ti,ab. (2010)

25 (pneumonia severity index or PSI or (PORT adj (score$ or scoring))).ti,ab. (21566)

26 19 or 20 or 21 or 22 or 23 or 24 or 25 (26187)

27 18 or 26 (284907)

28 11 and 27 (24815)

29 patient triage/ (3244)

30 (triage$ or triaging).ti,ab. (43825)

31 ((stratif$ or priorit$ or classif$) adj3 (patient$ or outpatient$)).ti,ab. (201540)

32 ((stratif$ or priorit$ or classif$) adj3 (symptom$ or sign? or illness$ or disease$ or disorder$ or severity or risk$)).ti,ab. (202687)

33 29 or 30 or 31 or 32 (406394)

34 11 and 33 (22210)

35 symptom assessment/ (11857)

36 patient acuity/ (1293)

37 ((initial or first or primary or point of care) adj3 (assess$ or evaluat$ or examin$ or screen$) adj3 (patient$ or outpatient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (22489)

38 ((sign? or symptom$) adj2 (score$ or scoring)).ti,ab. (51668)

39 ((assess$ or evaluat$ or determin$ or detect$ or analys$ or screen$) adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (46809)

40 ((patient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$) adj3 acuity).ti,ab. (11416)

41 35 or 36 or 37 or 38 or 39 or 40 (140927)

42 11 and 41 (15434)

43 clinical decision rule/ (684)

44 (clinical$ adj5 (decision$ or predicti$) adj5 (aid? or algorithm? or characteristic? or criteri$ or evaluation? or index or indices or marker? or method$ or model$ or panel? or parameter? or rule or rules or score? or scoring or screen$ or signs or symptoms or system? or technique? or test$ or tool? or value? or variable$)).mp. (62551)

45 (clinical$ adj (predicti$ or predictor$)).ti,ab. (18367)

46 (rule in or ruled in or rule out or ruled out).ti,ab. (93769)

47 (predict$ adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (14169)

48 ((predict$ or prognos$ or cluster$) adj3 (sign? or symptom$)).ti,ab. (39509)

49 43 or 44 or 45 or 46 or 47 or 48 (217048)

50 11 and 49 (15032)

51 28 or 34 or 42 or 50 (68399)

52 Health Economics/ (35574)

53 exp Economic Evaluation/ (352561)

54 exp Health Care Cost/ (336376)

55 pharmacoeconomics/ (9169)

56 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (1380284)

57 (expenditure$ not energy).ti,ab. (50208)

58 (value adj2 money).ti,ab. (2978)

59 budget$.ti,ab. (46855)

60 or/52-59 (1669816)

61 (metabolic adj cost).ti,ab. (1858)

62 ((energy or oxygen) adj cost).ti,ab. (5046)

63 ((energy or oxygen) adj expenditure).ti,ab. (37278)

64 60 not 63 (1666739)

65 51 and 64 (4185)

66 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (6800393)

67 65 not 66 (4080)

68 limit 67 to english language (3933)

69 (editorial or letter or note).pt. (3015508)

70 preprint.pt. (65307)

71 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (5535870)

72 or/69-71 (8616644)

73 68 not 72 (2705)

74 limit 73 to yr="2014 -Current" (1795)

75 remove duplicates from 74 (1705)

Key:

/ = indexing term (Emtree subject heading)

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$ = truncation

ti,ab = terms in either title or abstract fields

mp = multipurpose

db,pt,su = terms in database, publication type, or source type fields

? = wildcard for one additional letter

adj2 = terms within two words of each other (any order)

Econlit

via Ovid http://ovidsp.ovid.com/

Date range searched: <1886 to April 27, 2023>

Date searched: 15th May 2023

Records retrieved: 24

1 ((airway$ or bronchopulmonar$ or broncho-pulmonar$ or tracheobronch$ or tracheo-bronch$ or pulmonar$ tract or pulmonary or respirat$ tract or respiratory or chest or lung? or lobar or pleura?) adj3 (infect$ or coinfect$ or inflam$ or swollen or swelling$ or abscess$)).ti,ab. (107)

2 (bronchit$ or bronchiolit$ or allergic bronchopulmon$ or bronchopneumon$ or common cold$ or coryza or croup or empyem$ or epipharyngit$ or epiglottit$ or epiglotit$ or flu or influenza or laryngit$ or laryngotracheobronchit$ or laryngo tracheo bronchit$ or laryngo tracheobronchit$ or laryngotracheit$ or nasopharyngit$ or otitis media or parainfluenza or pharyngit$ or pleurisy or pneumoni$ or pleuropneumoni$ or rhinit$ or rhinopharyngit$ or rhinosinusit$ or severe acute respiratory syndrome or SARS or sinusit$ or sore throat$ or throat infection$ or supraglottit$ or supraglotit$ or tonsillit$ or tonsilit$ or tracheit$ or whooping cough or pertussis or pertusis).mp. (1282)

3 (ARTI or RTI or LRTI or URTI or ALRI or AURI or SARI).ti,ab. (67)

4 (glandular fever or Infectious Mononucleosis or Epstein-Barr).ti,ab. (0)

5 ((strep$ adj3 (throat$ or pharyn$ or tonsil$)) or (strep$ and (airway$ or pulmonary or brochopulmonar$ or brocho-pulmonar$ or respiratory$))).mp. (1)

6 ((acute$ or exacerbat$ or flare$) adj3 (copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway$ disease or chronic obstructive lung disease)).mp. (6)

7 ((acute$ or subacute$ or exacerbat$ or prolonged) adj3 cough$).mp. (2)

8 or/1-7 (1433)

9 (early warning$ or red flag$ or (flag$ adj2 early)).ti,ab. (1206)

10 (severity adj3 (score$ or scoring or scale$ or tool$ or instrument$ or index$ or indice$ or calculat$ or algorithm$ or metric$ or measur$ or criteri$ or code$)).ti,ab. (216)

11 (severity adj3 (assess$ or estimat$ or evaluat$ or classif$ or rate? or rating? or value? or quantif$ or grade$ or chart$ or equation$ or table$ or model$ or framework$ or predict$)).ti,ab. (280)

12 or/9-11 (1680)

13 (curb65 or crb65 or curb-65 or crb-65 or news2 or enews or pnews).ti,ab. (0)

14 ((curb or news) adj3 (criteri$ or rule$ or scor$ or predict$ or tool$)).ti,ab. (146)

15 CENTOR.ti,ab. (0)

16 (PMEWS or eMEWS).ti,ab. (0)

17 (McIsaac adj (score$ or scoring or criteri$)).ti,ab. (0)

18 (sino-nasal outcome test$ or SNOT-22 or SNOT22).ti,ab. (0)

19 (pneumonia severity index or PSI or (PORT adj (Score$ or scoring))).ti,ab. (165)

20 or/13-19 (311)

21 12 or 20 (1989)

22 8 and 21 (12)

23 (triage$ or triaging).ti,ab. (126)

24 ((stratif$ or priorit$ or classif$) adj3 (patient$ or outpatient$)).ti,ab. (145)

25 ((stratif$ or priorit$ or classif$) adj3 (symptom$ or sign? or illness$ or disease$ or disorder$ or severity or risk$)).ti,ab. (510)

26 or/23-25 (750)

27 8 and 26 (9)

28 ((initial or first or primary or point of care) adj3 (assess$ or evaluat$ or examin$ or screen$) adj3 (patient$ or outpatient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (18)

29 ((sign? or symptom$) adj2 (score$ or scoring)).ti,ab. (11)

30 ((assess$ or evaluat$ or determin$ or detect$ or analys$ or screen$) adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (25)

31 ((patient$ or sign? or symptom$ or illness$ or disease$ or disorder$ or infection$) adj3 acuity).ti,ab. (15)

32 or/28-31 (69)

33 8 and 32 (3)

34 (clinical$ adj5 (decision$ or predicti$) adj5 (aid? or algorithm? or characteristic? or criteri$ or evaluation? or index or indices or marker? or method$ or model$ or panel? or parameter? or rule or rules or score? or scoring or screen$ or signs or symptoms or system? or technique? or test$ or tool? or value? or variable$)).mp. (45)

35 (clinical$ adj (predicti$ or predictor$)).ti,ab. (3)

36 (rule in or ruled in or rule out or ruled out).ti,ab. (3585)

37 (predict$ adj5 (severe$ or severity or serious$) adj5 (sign? or symptom$ or illness$ or disease$ or disorder$ or infection$)).ti,ab. (13)

38 ((predict$ or prognos$ or cluster$) adj3 (sign? or symptom$)).ti,ab. (158)

39 or/34-38 (3801)

40 8 and 39 (4)

41 22 or 27 or 33 or 40 (24)

42 remove duplicates from 41 (24)

Key:

$ = truncation

ti,ab = terms in either title or abstract fields

mp = multipurpose

? = wildcard for one additional letter

adj2 = terms within two words of each other (any order)

NHS Economic Evaluation Database (NHS EED)

via CRD https://www.crd.york.ac.uk/CRDWeb/HomePage.asp

Date range searched: Inception to 31st March 2015

Date searched: 15th May 2023

Records retrieved: 126

1 MeSH DESCRIPTOR Respiratory Tract Infections EXPLODE ALL TREES IN NHSEED 582

2 ((airway* or bronchopulmonar* or broncho-pulmonar* or tracheobronch* or tracheo-bronch* or pulmonar* tract or pulmonary or respirat* tract or respiratory or chest or lung* or lobar or pleura*) NEAR4 (infect* or coinfect* or inflam* or swollen or swelling* or abscess*)) IN NHSEED 178

3 (bronchit* or bronchiolit* or allergic bronchopulmon* or bronchopneumon* or common cold* or coryza or croup or empyem* or epipharyngit* or epiglottit* or epiglotit* or flu or influenza or laryngit* or laryngotracheobronchit* or laryngo tracheo bronchit* or laryngo tracheobronchit* or laryngotracheit* or nasopharyngit* or otitis media or parainfluenza or pharyngit* or pleurisy or pneumoni* or pleuropneumoni* or rhinit* or rhinopharyngit* or rhinosinusit* or severe acute respiratory syndrome or SARS or sinusit* or sore throat* or throat infection* or supraglottit* or supraglotit* or tonsillit* or tonsilit* or tracheit* or whooping cough or pertussis or pertusis) IN NHSEED 826

4 (ARTI or RTI or LRTI or URTI or ALRI or AURI or SARI) IN NHSEED 29

5 MeSH DESCRIPTOR Infectious Mononucleosis IN NHSEED 0

6 (glandular fever or Infectious Mononucleosis or Epstein-Barr) IN NHSEED 3

7 ((strep* NEAR4 (throat* or pharyn* or tonsil*)) or (strep* and (airway* or pulmonary or brochopulmonar* or brocho-pulmonar* or respiratory*))) IN NHSEED 22

8 ((acute* or exacerbat* or flare*) NEAR4 (copd or coad or chronic obstructive pulmonary disease or chronic obstructive airway* disease or chronic obstructive lung disease)) IN NHSEED 27

9 ((acute* or subacute* or exacerbat* or prolonged) NEAR4 cough*) IN NHSEED 3

10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 1057

11 MeSH DESCRIPTOR early warning score IN NHSEED 0

12 MeSH DESCRIPTOR "Severity of Illness Index" IN NHSEED 0

13 (early warning* or red flag* or (flag* NEAR3 early)) IN NHSEED 5

14 (severity NEAR4 (score* or scoring or scale* or tool* or instrument* or index* or indice* or calculat* or algorithm* or metric* or measur* or criteri* or code*)) IN NHSEED 660

15 (severity NEAR4 (assess* or estimat* or evaluat* or classif* or rate* or rating* or value* or quantif* or grade* or chart* or equation* or table* or model* or framework* or predict*)) IN NHSEED 88

16 #11 or #12 or #13 or #14 or #15 709

17 (curb65 or crb65 or curb-65 or crb-65 or news2 or enews or pnews) IN NHSEED 0

18 ((curb or news) NEAR4 (criteri* or rule* or scor* or predict* or tool*)) IN NHSEED 0

19 CENTOR IN NHSEED 5

20 (PMEWS or eMEWS) IN NHSEED 0

21 (McIsaac NEAR1 (score* or scoring or criteri*)) IN NHSEED 0

22 (sino-nasal outcome test* or SNOT-22 or SNOT22) IN NHSEED 0

23 (pneumonia severity index or PSI or (PORT NEAR1 (Score* or scoring))) IN NHSEED 9

24 #17 or #18 or #19 or #20 or #21 or #22 or #23 14

25 #16 or #24 719

26 #10 and #25 55

27 MeSH DESCRIPTOR Triage IN NHSEED 47

28 (triage* or triaging) IN NHSEED 111

29 ((stratif* or priorit* or classif*) NEAR4 (patient* or outpatient*)) IN NHSEED 107

30 ((stratif* or priorit* or classif*) NEAR4 (symptom* or sign* or illness* or disease* or disorder* or severity or risk*)) IN NHSEED 179

31 #27 or #28 or #29 or #30 368

32 #10 and #31 24

33 MeSH DESCRIPTOR Symptom Assessment IN NHSEED 0

34 MeSH DESCRIPTOR Patient Acuity IN NHSEED 5

35 ((initial or first or primary or point of care) NEAR4 (assess* or evaluat* or examin* or screen*) NEAR4 (patient* or outpatient* or sign* or symptom* or illness* or disease* or disorder* or infection*)) IN NHSEED 65

36 ((sign* or symptom*) NEAR3 (score* or scoring)) IN NHSEED 153

37 ((assess* or evaluat* or determin* or detect* or analys* or screen*) NEAR6 (severe* or severity or serious*) NEAR6 (sign* or symptom* or illness* or disease* or disorder* or infection*)) IN NHSEED 109

38 ((patient* or sign* or symptom* or illness* or disease* or disorder* or infection*) NEAR4 acuity) IN NHSEED 27

39 #33 or #34 or #35 or #36 or #37 or #38 346

40 #10 and #39 27

41 MeSH DESCRIPTOR Clinical Decision Rules IN NHSEED 0

42 (clinical* NEAR6 (decision* or predicti*) NEAR6 (aid* or algorithm* or characteristic* or criteri* or evaluation* or index or indices or marker* or method* or model* or panel* or parameter* or rule or rules or score* or scoring or screen* or signs or symptoms or system* or technique* or test* or tool* or value* or variable*)) IN NHSEED 199

43 (clinical* NEAR1 (predicti* or predictor*)) IN NHSEED 12

44 (rule in or ruled in or rule out or ruled out) IN NHSEED 174

45 (predict* NEAR6 (severe* or severity or serious*) NEAR6 (sign* or symptom* or illness* or disease* or disorder* or infection*)) IN NHSEED 4

46 ((predict* or prognos* or cluster*) NEAR4 (sign* or symptom*)) IN NHSEED 23

47 #41 or #42 or #43 or #44 or #45 or #46 401

48 #10 and #47 41

49 #26 or #32 or #40 or #48 126

Key:

MeSH DESCRIPTOR = indexing term (Medical Subject Heading: MeSH)

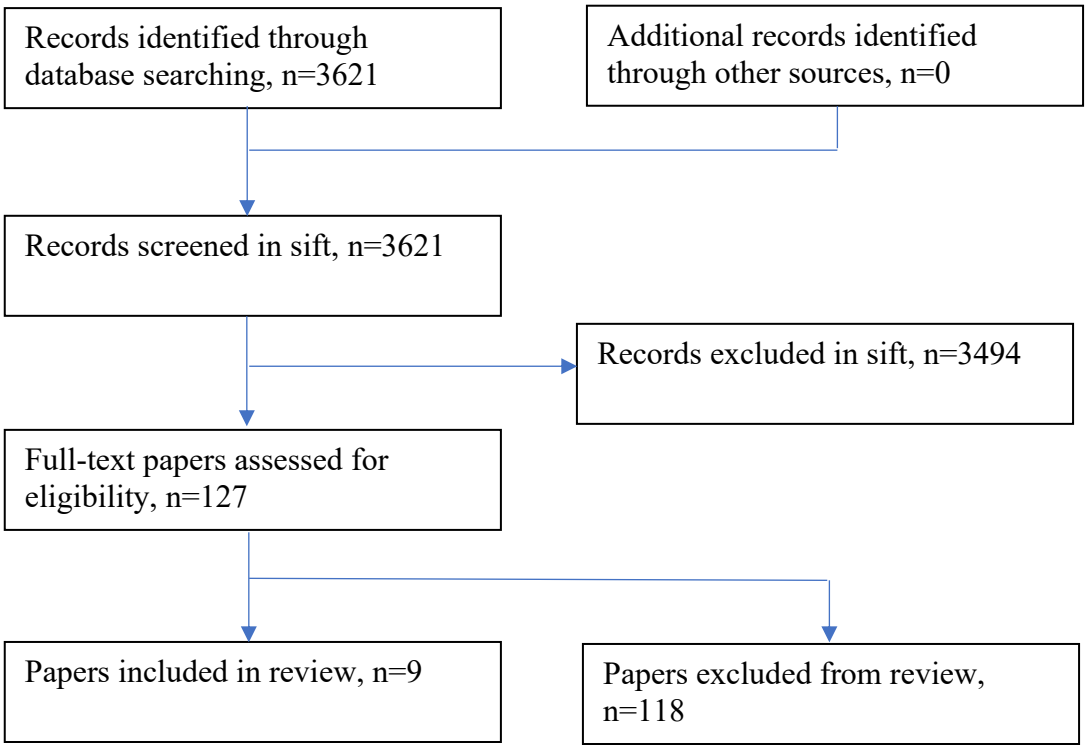
EXPLODE ALL TREES = exploded indexing term (MeSH)

NEAR4 = terms within four words of each other (specified order only)

* = truncation

Appendix C – Clinical evidence study selection

Figure 1: Flow chart of clinical study selection for the review of signs, symptoms and early warning scores for predicting severe illness in the initial assessment of people aged 16 years or over with suspected acute respiratory infection



Appendix D – Clinical evidence

Aalbers, 2011

Bibliographic Reference	Aalbers J, O'Brien K K, Chan W S et al. Predicting streptococcal pharyngitis in adults in primary care: a systematic review of the diagnostic accuracy of symptoms and signs and validation of the Centor score. BMC Medicine 2011; 9:67

Study details

Study type	Systematic review
Study location	Included studies were from USA, Canada, Europe, New Zealand, Thailand, Israel
Study setting	Primary care (19 studies) and the emergency department (2 studies)
Study dates	PubMed and EMBASE were searched to 26 July 2010; included studies were published between 1975 and 2008
Sources of funding	Health Research Board of Ireland through the HRB Centre for Primary Care Research
Review question	To analyse the current evidence on the usefulness of individual signs and symptoms in assessing the risk of streptococcal pharyngitis in adults, to assess the diagnostic accuracy of the Centor score as a decision rule for antibiotic treatment (discrimination analysis) and to perform a meta-analysis on validation studies of the Centor score (calibration analysis).
Inclusion criteria	Studies were included if participants were recruited upon first presentation from an ambulatory care setting, had a sore throat as their main presenting complaint, and were ≥15 years of age. Both prospective and retrospective studies were included. Each included study assessed the diagnostic accuracy of signs and symptoms and/or validated the Centor score.
Exclusion criteria	Not reported
Study design of included studies	Diagnostic accuracy studies
Sample size	21 included studies, comprising 4,839 patients (range 70 to 693), reported data on signs and symptoms. 15 included studies, comprising 2,900 patients (range 70 to 453), reported data on the Centor score.
Quality of included studies	The overall quality of the included studies was good, assessed using a modified version of the QUADAS tool. The spectrum of patients was generally appropriate and representative, selection criteria were stated and the signs and symptoms were generally clearly described. Test and diagnostic review bias items scored well. Observer variation in assessing signs and symptoms was poorly reported.
Target condition/ outcome	Group A β-haemolytic streptococcal (GABHS) pharyngitis
Patient characteristics	Mean age: range 23.9 to 35.6 years (where reported) Sex: range 16.7% to 63.6% male (where reported) Prevalence of GABHS pharyngitis: range 4.7% to 37.6%

Signs, symptoms and early warning scores	Individual signs and symptoms: • Absence of cough • Fever • Anterior cervical adenopathy • Tender anterior cervical adenopathy • Any exudates (either tonsillar exudate or pharyngeal exudate or any exudate) Centor score
Comparator/ reference standard	Throat culture
Results	<u>Absence of cough (19 studies, 4,653 patients)</u> Sensitivity (95% CI): 0.74 (0.68 to 0.79) Specificity (95% CI): 0.49 (0.40 to 0.58) Positive likelihood ratio (95% CI): 1.46 (1.28 to 1.66) Negative likelihood ratio (95% CI): 0.53 (0.46 to 0.61) <u>Fever (21 studies, 4,635 patients; the most widely used cut-off to indicate fever was 38.0°C)</u> Sensitivity (95% CI): 0.50 (0.39 to 0.62) Specificity (95% CI): 0.70 (0.58 to 0.79) Positive likelihood ratio (95% CI): 1.65 (1.40 to 1.95) Negative likelihood ratio (95% CI): 0.71 (0.64 to 0.80) <u>Anterior cervical adenopathy (9 studies, 2,101 patients)</u> Sensitivity (95% CI): 0.65 (0.55 to 0.74) Specificity (95% CI): 0.55 (0.45 to 0.64) Positive likelihood ratio (95% CI): 1.45 (1.25 to 1.67) Negative likelihood ratio (95% CI): 0.63 (0.52 to 0.76) <u>Tender anterior cervical adenopathy (16 studies, 4,144 patients</u> Sensitivity (95% CI): 0.67 (0.52 to 0.79) Specificity (95% CI): 0.59 (0.49 to 0.69) Positive likelihood ratio (95% CI): 1.65 (1.41 to 1.92) Negative likelihood ratio (95% CI): 0.56 (0.41 to 0.76) <u>Any exudates (21 studies, 4,839 patients)</u> Sensitivity (95% CI): 0.57 (0.44 to 0.70) Specificity (95% CI): 0.74 (0.63 to 0.82) Positive likelihood ratio (95% CI): 2.20 (1.76 to 2.74) Negative likelihood ratio (95% CI): 0.58 (0.47 to 0.72) <u>Centor score ≥1 (11 studies)</u> Sensitivity (95% CI): 0.95 (0.91 to 0.97) Specificity (95% CI): 0.18 (0.12 to 0.26) Positive likelihood ratio (95% CI): 1.16 (1.08 to 1.25)

	Negative likelihood ratio (95% CI): 0.27 (0.16 to 0.46) Centor score ≥2 (12 studies) Sensitivity (95% CI): 0.79 (0.71 to 0.86) Specificity (95% CI): 0.55 (0.45 to 0.65) Positive likelihood ratio (95% CI): 1.76 (1.51 to 2.07) Negative likelihood ratio (95% CI): 0.37 (0.29 to 0.48) Centor score ≥3 (the recommended cut-off point for empirical antibiotic treatment according to the ACP/ASIM guidelines) (11 studies) Sensitivity (95% CI): 0.49 (0.38 to 0.60) Specificity (95% CI): 0.82 (0.72 to 0.88) Positive likelihood ratio (95% CI): 2.68 (1.92 to 3.75) Negative likelihood ratio (95% CI): 0.62 (0.52 to 0.74) Centor score 4 (11 studies) Sensitivity (95% CI): 0.18 (0.12 to 0.27) Specificity (95% CI): 0.95 (0.92 to 0.97) Positive likelihood ratio (95% CI): 3.85 (2.05 to 7.24) Negative likelihood ratio (95% CI): 0.86 (0.78 to 0.93) Post-test probability of GABHS pharyngitis for a range of pre-test probabilities

Points	Likelihood ratio	Pretest probability of GABHS pharyngitis (%)							
		5	**10**	**15**	**20**	**25**	**30**	**35**	**40**
≥1	1.16	6	11	17	22	28	33	38	44
≥2	1.76	8	16	24	31	37	43	49	54
≥3	2.68	12	23	32	40	47	53	59	64
4	3.85	17	30	40	49	56	62	67	72

Authors' conclusion	Individual symptoms and signs have only a modest ability to rule in or out a diagnosis of GABHS pharyngitis. The Centor score uses a combination of signs and symptoms to predict the risk of GABHS pharyngitis; the score is well calibrated across a variety of countries and settings. It has reasonably good specificity, and can enhance the appropriate prescribing of antibiotics, but should be used with caution in low prevalence settings of GABHS pharyngitis such as primary care.
Limitations	Prevalence of GABHS pharyngitis varied widely between the included studies (range 4.7% to 37.6%), however, the authors undertook a subgroup analysis based on prevalence for each score category of the Centor score. Whilst not explicitly stated, the conclusion relating to the reasonably high specificity of the Centor score relates to the cut-off score of ≥3, which is the recommended cut-off point for empirical antibiotic treatment according to the ACP/ASIM guidelines.
Comments	There was a low risk of bias for each ROBIS domain. The conclusions of the review appear to be appropriate, noting the authors' caution relating to the use of the Centor score when used as a decision aid for antibiotic prescribing.

Critical appraisal – ROBIS tool

Overall risk of bias	Low
Applicability as a source of data	Good

Akram, 2011

Bibliographic Reference	Akram A R, Chalmers J D and Hill A T. Predicting mortality with severity assessment tools in out-patients with community-acquired pneumonia. Q J Med 2011; 104:871-9

Study details

Study type	Systematic review
Study location	Included studies were from USA, Canada, Netherlands, Germany, Spain, France, UK
Study setting	Outpatients (either exclusively managed in the community or discharged from an emergency department <24 hours after admission)
Study dates	Medline and EMBASE were searched between 1981 and 2010; included studies were published between 1997 and 2008
Sources of funding	One of the authors was supported by a Clinical Research Training Fellowship from the Medical Research Council
Review question	To systematically review the published literature in relation to pneumonia scoring systems (such as the Pneumonia severity index [PSI] and CURB65/CRB65) for predicting mortality in patients managed in outpatient settings
Inclusion criteria	Studies were included if they reported data (calculation of severity score based on admission data) on at least 20 unselected outpatients with community acquired pneumonia. There were no inclusion/exclusion criteria relating to study design.
Exclusion criteria	Non-CAP diagnoses (e.g. non-pneumonic exacerbation of COPD)
Study design of included studies	Nine prospective cohort studies, one retrospective case review and three randomised controlled trials
Sample size	13 included studies, comprising 5,444 patients (range 48 to 1061)
Quality of included studies	Overall, six studies were rated as good, five as moderate and two as suboptimal, using the following criteria: (i) inclusion: patients recruited consecutively and in an unbiased fashion according to a standard definition of CAP; (ii) follow-up: were the patients appropriately followed up to determine survival; (iii) severity score measurement: severity score calculated according to standard definition and calculated at presentation; and (iv) potential confounding: potential confounders considered and accounted for.
Target condition/ outcome	30-day mortality
Patient characteristics	Mean age: range 46.8 to 77.3 (where reported) Sex: Not reported Mortality rate: range 0 to 3.5%
Signs, symptoms and early warning scores	PSI (10 studies) CRB65 (4 studies) CURB65 (2 studies)

Comparator/ reference standard	Not applicable
Results	PSI (10 studies, 3972 patients) PSI I-III (low risk): 0.2% mortality (8 of 3655 patients) PSI IV-V (high risk): 10.1% mortality (32 of 317 patients) Comparing low against high risk (6 studies): Pooled sensitivity = 92% (64-100%), pooled specificity = 90% (89-91%). Negative likelihood ratio (NLR) = 0.21 (0.08-0.59). Area under the sROC = 0.92 (SE 0.03). The risk of death in low-risk patients (PSI I-III) was compared to the pre-set 1% predicted level of mortality, PSI had a relative risk of 0.35 (0.17-0.72) with no significant heterogeneity. CRB65 (4 studies, 1648 patients) CRB65=0: 0% mortality (879 patients) CRB65=1: 0.5% mortality (615 patients) CRB65=2: 6.3% mortality (126 patients) CRB65=3: 13.2% mortality (28 patients) CRB65=4: No patients in this category Requirement for hospitalisation: Using the recommended cut-off of CRB65>0, pooled sensitivity = 100% (48-100%), pooled specificity = 65% (62-68%), with no significant heterogeneity (3 studies). Using CRB65>1, pooled sensitivity = 81% (54-96%), pooled specificity = 91% (90-93%). Area under the sROC = 0.91 (SE 0.05). Pooled diagnostic odds ratio for a CRB65 score ≥2 = 16.47 (4.9-55.4) with no significant heterogeneity. Estimates were limited by low event rate. Comparing the performance of CRB65 in patients with CRB65 0 to 1 (low-risk patients) to the pre-set 1% level of mortality, CRB65 was associated with a relative risk of 0.35 (0.10-1.16) with no significant heterogeneity. CURB65 (2 studies; therefore, meta-analysis not feasible) One study reported data in 676 outpatients and one study reported data in 176 outpatients; each study had one death in the outpatient group and both with CURB65 ≥2.
Authors' conclusion	Patients in the low risk CRB65 and PSI classes are at low risk of death when managed as out-patients but further studies are needed in out-patient cohorts
Limitations	The majority of the data presented were derived from patients initially assessed in hospital and discharged within 24 hours; the authors acknowledge that this is a significant limitation of the analysis and further studies in exclusively out-patient populations are required. The authors also comment on a number of potential confounders that must be considered; patient factors such as patient preference for out-patient care may lead to more high-risk patients being managed as out-patients and there may be a number of patients where CAP may be seen as a terminal event and a decision made against hospitalisation given prognostic considerations, therefore, some of the mortality observed in out-patients is likely to represent patients in whom hospitalisation was deemed inappropriate.
Comments	There was a low risk of bias for each ROBIS domain. The conclusions of the review appear to be appropriate, noting the authors' caution relating to the need for further studies in exclusively out-patient cohorts (as opposed to patients initially assessed in hospital and discharged within 24 hours).

Critical appraisal – ROBIS tool

Overall risk of bias	Low
Applicability as a source of data	Good

Chalmers, 2011

Bibliographic Reference	Chalmers J D, Akram A R and Hill A T. Increasing outpatient treatment of mild community-acquired pneumonia: systematic review and meta-analysis. European Respiratory Journal 2011; 37:858-64

Study details

Study type	Systematic review
Study location	Included studies were from USA, Canada, Spain and France
Study setting	Emergency departments (5 studies) and walk-in medical centres (1 study)
Study dates	PubMed and EMBASE were searched between January 1981 and April 2010; included studies were published between 1998 and 2007
Sources of funding	One of the authors was supported by a Clinical Research Training Fellowship from the Medical Research Council (UK)
Review question	To identify, synthesise and interpret the evidence relating to strategies to increase the proportion of low-risk patients with CAP treated in the community
Inclusion criteria	Studies were included if they described an intervention aimed to increase the proportion of patients treated in the community, included a control group in which the intervention was withheld and included data reporting the safety of the intervention
Exclusion criteria	Studies reporting outpatient care but without control data were not included
Study design of included studies	Randomised controlled trials; implementation studies with either a prospective or retrospective control group; prospective observational study with control
Sample size	6 included studies, comprising 5,092 patients (range 223 to 1,901)
Quality of included studies	The authors state that quality was assessed using standardised criteria and reference the Cochrane Handbook. They state that all of the included studies had significant limitations. Two studies used a retrospective control cohort design, which is associated with a significant risk of bias. In one study the centres were not randomised, but decided independently to implement the PSI or not, with no way of knowing what other aspects of CAP management differed between centres. Two cluster randomised controlled trials were more robust, however, randomisation at the hospital level cannot ensure that PSI was not used at the individual-physician level in the control hospitals. The final study was more robust but was underpowered to detect mortality.
Target condition/ outcome	Proportion of patients treated as outpatients, mortality, hospital re-admissions, patient satisfaction with care, health-related quality of life and return to work or usual activities
Patient characteristics	Not reported.
Signs, symptoms and early warning scores	The interventions were generally complex, but all included a scoring system to identify low-risk patients; in five studies the PSI was used to help determine where patients should be treated, in one study the authors derived their own criteria for in-patient care
Comparator/ reference standard	Usual care (prospective or retrospective control group) or low-intensity guideline implementation (vs moderate- or high-intensity)

Results	Five studies (4,869 patients) were included in the meta-analysis for outpatient care (the other study randomised patients to out- or in-patient care, rather than implementing a guideline to increase the proportion of patients treated in the community); 64.6% of patients in the intervention groups were treated in the community compared with 48.7% of patients in the control groups. The interventions were associated with a significant increase in outpatient-managed patients (OR: 2.31, 95% CI: 2.03 to 2.63), there was no significant heterogeneity. Mortality was not increased in the intervention groups (OR: 0.83, 95% CI: 0.59 to 1.17; 6 studies). There was no increase in hospital readmissions (OR: 1.08, 95% CI: 0.82 to 1.42; 6 studies). There was no difference in patient satisfaction with care between intervention and control groups (OR: 1.21, 95% CI: 0.97 to 1.49; 3 studies). There was no significant heterogeneity in these analyses. There were insufficient data to pool studies of return to usual activities or quality of life. One study reported no significant difference between intervention and control groups in return to usual activities, or in patients reporting excellent or very good general health at four weeks. Two studies assessed quality of life using Short-Form 36 and reported no significant difference between intervention and control groups. One study reported no significant difference in return to work and usual activities at day 30 between groups.
Authors' conclusion	Current evidence suggests that strategies to increase the proportion of patients treated in the community are safe, effective and acceptable to patients
Limitations	Each study included in the review had significant methodological limitations. The interventions included in the studies were generally complex, the scoring system to identify low-risk patients was only one component and, as acknowledged by the authors, evaluating which components of the intervention were responsible for the effects seen is not straightforward.
Comments	There was a low risk of bias for each ROBIS domain. The conclusions of the review appear to be appropriate. However, the scoring system to identify low-risk patients was only one component of the interventions assessed.

Critical appraisal – ROBIS tool

Overall risk of bias	Low
Applicability as a source of data	Acceptable (scoring system to identify low-risk patients was only one component of the interventions assessed)

Dosa, 2005

Bibliographic Reference	Dosa D. Should I hospitalize my resident with nursing home-acquired pneumonia? Journal of the American Medical Directors Association 2005; 6:327-33

Study details

Study type	Systematic review
Study location	Included studies were from USA
Study setting	Nursing home
Study dates	Medline was searched between 1966 and 'present day'; included studies were published between 1998 and 2001
Sources of funding	Not reported
Review question	Are there prediction tools that can help determine when treating a resident in the nursing home is safe?
Inclusion criteria	The author performed a structured search relating to the diagnosis, treatment and triage of residents with nursing home acquired pneumonia (NHAP). There were no inclusion/exclusion criteria relating to study design.
Exclusion criteria	Not reported
Study design of included studies	One prospective cohort study and two retrospective studies (relating to the question of interest)
Sample size	3 included studies, comprising 1,942 cases/episodes (range 158 to 1406)
Quality of included studies	Not reported (studies do not appear to have been assessed for quality)
Target condition/ outcome	30-day mortality
Patient characteristics	Not reported
Signs, symptoms and early warning scores	PSI 5-point scale developed by Naughton and Mylotte 8-variable model developed by Mehr et al.
Comparator/ reference standard	Not applicable
Results	<u>PSI (1 study, 158 episodes)</u> Similar reliability to that in patients with community-acquired pneumonia. However, 85% of nursing home residents were classified as high risk (class IV or V) requiring hospitalisation, making the PSI a poor discriminatory tool in the nursing home environment. Additionally, the difficulty in obtaining arterial blood gas measurements in the nursing home setting has severely limited its use.

	5-point scale developed by Naughton and Mylotte (1 study, 378 cases) Analysis of a retrospective chart review revealed four predictors of mortality developed into a 5-point scale: respiratory rate greater than 30 (2 points), pulse rate greater than 125 (1 point), change in mental status (1 point) and the presence of dementia (1 point). Applying this model to each episode in the derivation cohort revealed an increase in mortality with increasing score. Prospective validation of this model, however, has not been documented. This model does hold promise, however, as it uses variables that are easy to collect in an acute setting and does not rely on laboratory/radiographic testing. 8-variable model developed by Mehr et al. (1 study, 1406 episodes amongst 1044 residents) A model was developed using a prospective cohort, based on levels of serum urea nitrogen (BUN), white blood count, absolute lymphocyte count, heart rate, sex, body mass index, activities of daily living, and mood deterioration in last 90 days. Independent validation of this model has not been achieved and measures common to other predictive models, including respiratory rate, were not included. Likewise, pulse oximetry readings were also not included. Nevertheless, the Mehr et al. model is unique because it represents a large, multifacility trial conducted in typical community nursing homes as opposed to academic nursing homes.
Author's conclusion	While prediction models will likely prove to be useful in decision tree analysis, there are numerous problems with using the current models in clinical practice. First, while probability models may predict mortality risk, they do not answer the basic question of whether a resident's care, given a particular severity, is better or worse with transfer to the hospital. Second, the models described above are generally age-driven, conveying the highest risk on those at advanced age. Nursing home residents are generally very old, thereby eliminating one of the most discriminating features of the probability model. Third, existing models do not incorporate the resident's end-of-life wishes or overall goals of care. Finally, current models for predicting mortality require data collection that is often not readily available at the time that triage decisions need to be made.
Limitations	This was a poorly conducted and reported systematic review, addressing multiple questions including the one of interest here. It is unclear whether all relevant studies were identified, the quality of the studies was not systematically assessed and limited details of the included studies were presented.
Comments	There was a high risk of bias for each ROBIS domain. The author's conclusions appear appropriate based on the included studies, however, in view of the considerable risk of bias, they may not be reliable.

Critical appraisal – ROBIS tool

Overall risk of bias	High (poorly conducted and reported review, it is unclear whether all relevant studies were identified, the quality of included studies was not assessed and

	limited details of included studies were presented)
Applicability as a source of data	Good

Ebell, 2019

Bibliographic Reference	Ebell M H, Walsh M E, Fahey T et al. Meta-analysis of calibration, discrimination, and stratum-specific likelihood ratios for the CRB-65 score. Journal of General Internal Medicine 2019; 34:1304-13

Study details

Study type	Systematic review/meta-analysis update of McNally et al., 2010
Study location	Not fully reported. All but 3 studies were set in Europe, including 10 in Germany and 6 in Spain; none were set in the USA or Canada.
Study setting	Hospitalised patients, ambulatory patients and both; the 15 studies that included ambulatory patients in emergency department or primary care settings are relevant to this review
Study dates	PubMed was searched from January 2009 to update a previous systematic review that searched up to June 2009; included studies were published between 2006 and 2015
Sources of funding	One of the authors was supported by a 2018/2019 Fulbright Teaching/Research award
Review question	To perform an updated meta-analysis of the accuracy of the CRB-65 for mortality prediction
Inclusion criteria	Studies reporting the accuracy of the CRB-65 score among patients with community acquired pneumonia (CAP). Studies had to provide sufficient data to calculate mortality for low-risk, moderate-risk and high-risk groups. Both prospective and retrospective cohort studies were included.
Exclusion criteria	Studies in children, studies in special populations (such as immunocompromised patients or those characterised by a comorbidity such as asthma, cancer, or diabetes), and studies of patients with sepsis, hospital-acquired or ventilator-acquired pneumonia were excluded. Studies performed in countries classified as low income or lower-middle income, and case control studies.
Study design of included studies	Nine studies gathered data retrospectively, while the remainder gathered data prospectively, often as part of the CAPNETZ disease registry
Sample size	29 included studies, comprising 1,089,419 patients (range 105 to 669,594). 13 studies where the rule was applied in both hospitalised and ambulatory settings included 20,282 patients (range 152 to 6,142). Two studies in ambulatory settings included 956 patients (range 314 to 642).
Quality of included studies	Overall, 12 studies were judged to be at low risk of bias and 17 studies were judged to be at high risk of bias, using an adaptation of the TRIPOD and PROBAST criteria. Of the 15 studies where the rule was applied in emergency department or primary care settings 7 were judged to be at low risk of bias and 8 were judged to be a high risk of bias.
Target condition/ outcome	30-day mortality
Patient characteristics	Mean or median age: range 36.5 to 78.3 Sex: Not reported Mortality rate: range 0.5% to 18.0%

Signs, symptoms and early warning scores	CRB-65
Comparator/ reference standard	Not applicable
Results	<u>Subgroup analysis of studies where the rule was applied in emergency department or primary care settings and patients could be treated as either outpatients or inpatients</u> Summary estimate of Observed/Expected (*O:E*) ratio: 1.05 (95% CI: 0.87 to 1.27); 15 studies (n=20,667 patients), I^2=91.3% Area Under the Receiver Characteristic Curve (AUC): 0.75 (95% CI: 0.71 to 0.78); 13 studies (n=14,373 patients), I^2=85.1% Stratum-specific likelihood ratios: CRB-65=0 (low risk): 0.12 (95% CI: 0.07 to 0.19; 11 studies, I^2: 34.6%) CRB-65=1-2 (moderate risk): 1.10 (95% CI: 0.96 to 1.25; 15 studies, I^2: 93.8%) CRB-65=3-4 (high risk): 5.59 (95% CI: 4.25 to 7.34; 15 studies, I^2: 75.6%) <u>Subgroup analysis of studies at low risk of bias where the rule was applied in emergency department or primary care settings and patients could be treated as either outpatients or inpatients</u> Summary estimate of Observed/Expected (*O:E*) ratio: 0.88 (95% CI: 0.69 to 1.13); 8 studies (n=17,248 patients), I^2=92.7% Area Under the Receiver Characteristic Curve (AUC): 0.76 (95% CI: 0.70 to 0.81); 17 studies (n=11,106 patients), I^2=91.0% Stratum-specific likelihood ratios: CRB-65=0 (low risk): 0.13 (95% CI: 0.08 to 0.21; 8 studies, I^2: 40.0%) CRB-65=1-2 (moderate risk): 1.30 (95% CI: 1.17 to 1.44; 8 studies, I^2: 84.7%) CRB-65=3-4 (high risk): 5.61 (95% CI: 3.71 to 8.47; 8 studies, I^2: 85.6%)
Authors' conclusion	The CRB-65 can be used by physicians to estimate mortality risk, and can serve as a useful check on physician judgement. Patients in the low-risk group with a score of 0 have a very low mortality risk (0.5% given a typical mortality rate of 4% for CAP) and can in most cases safely be treated as outpatients. Most patients in the moderate- and high-risk groups should be hospitalised, although other considerations may alter these decisions regarding treatment setting.
Limitations	The majority of studies included in the subgroup analyses of studies where the rule was applied in emergency department or primary care settings included both hospitalised and ambulatory patients, only 2 studies included only ambulatory patients. There was significant heterogeneity between studies.
Comments	There was a low risk of bias for most ROBIS domains; although the domain relating to the identification and selection of studies had a high risk of bias, as the authors only searched PubMed and the first 100 articles on Google Scholar (along with reference lists of included articles). The authors' conclusions appear

	to be appropriate, although as acknowledged by the authors there was significant heterogeneity for the higher risk subgroups.

Critical appraisal – ROBIS tool

Overall risk of bias	High (Limited search strategy; it is unclear whether all relevant studies were identified)
Applicability as a source of data	Acceptable (most studies where the rule was applied in emergency department or primary care settings included both hospitalised and ambulatory patients)

McNally, 2010

Bibliographic Reference	McNally M, Curtain J, O'Brien KK et al. Validity of British Thoracic Society guidance (the CRB-65 rule) for predicting the severity of pneumonia in general practice: systematic review and meta-analysis. British Journal of General Practice 2010; 60:e423-33

Study details

Study type	Systematic review (this review has been updated by Ebell et al., 2019)
Study location	Not reported
Study setting	Hospitalised patients, emergency department, primary care patients and patients treated as outpatients; the 4 studies that included primary care patients and patients treated as outpatients are relevant to this review
Study dates	PubMed (from 1966 to June 2009), Medline, EMBASE and the Cochrane Library were searched; included studies were published between 2006 and 2009
Sources of funding	One of the authors was supported by an RCSI Research Studentship, two authors were supported by the HRB Centre for Primary Care Research
Review question	To determine the accuracy of CRB-65 in predicting 30-day mortality and assess how well it performs in community and hospital settings
Inclusion criteria	Cohort studies of community-based or hospital-based adults (≥16 years) with a primary diagnosis of community acquired pneumonia, in which CRB-65 score was calculated, and death within 30 days was reported, were eligible
Exclusion criteria	Not reported
Study design of included studies	Eight prospective cohort studies, three retrospective analyses of prospectively collected data, one retrospective cohort study, one longitudinal cohort study and one study reporting pooled data from two randomised controlled trials. Three of the four studies relevant to this review were prospective cohort studies and one was a retrospective analysis of a prospective consecutive cohort.
Sample size	14 included studies, comprising 397,875 patients (range 105 to 388,406). The 4 studies which included primary care patients and patients treated as outpatients included 1817 community-based patients (range 314 to 676).
Quality of included studies	Quality was assessed following the methodological standard of McGinn for validation studies of clinical prediction rules. In 11 studies patients were chosen in an unbiased fashion, but in 2 studies they were not and in one study it was unclear. Patients represented a wide spectrum of disease in 6 studies, but not in 8 studies. Only 2 studies reported blinded assessment of the rule criteria for all patients; this was unclear in 12 studies. There was an explicit and accurate interpretation of the predictor variables and the actual rule without knowledge of the outcome in all studies. There was 100% follow-up in 3 studies, but not in 7 studies and this was unclear in 4 studies.
Target condition/ outcome	30-day mortality
Patient characteristics	Mean/median age: range 60.4 to 77.3 (where reported) Sex: Proportion male was not reported Mortality rate: Not reported

Signs, symptoms and early warning scores	CRB-65
Comparator/ reference standard	The initial derivation study of the CRB-65 rule was used as the predictive model to which all validation studies were compared
Results	Amongst community-based patients, 54.4% of patients (n=1025) were in the low-risk category and there were 0 mortality events (risk ratio 9.41, 95% CI: 1.75 to 50.66; 3 studies, I^2=0%). 43.6% of patients (n=765) were in the intermediate-risk group, with 1.6% mortality events (risk ratio 4.84, 95% CI: 2.61 to 8.96; 4 studies, I^2=0%). 1.9% of patients (n=27) were in the high-risk group, with 18.5% mortality events (risk ratio 1.58, 95% CI 0.59 to 4.19; 3 studies, I^2=0%).
Authors' conclusion	CRB-65 has not been validated sufficiently in primary care settings and preliminary findings suggest over-prediction, so its value as a prognostic indicator in the community remains uncertain
Limitations	The authors acknowledge that low event rates make precise estimates about CRB-65 performance less certain
Comments	There was a low risk of bias for each ROBIS domain. The conclusions of the review appear to be appropriate.

Critical appraisal – ROBIS tool

Overall risk of bias	Low
Applicability as a source of data	Good

Metlay, 2019

Bibliographic Reference	Metlay J P, Waterer G W, Long A C et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. American Journal of Respiratory & Critical Care Medicine 2019; 200:e45-67

Study details

Study type	Systematic review
Study location	Not reported
Study setting	Not reported, however, studies assessed initial site of treatment and requirement for hospitalisation
Study dates	PubMed was searched on a monthly basis between 2015 and 2017; included studies were published between 1998 and 2015
Sources of funding	Supported by the American Thoracic Society and Infectious Diseases Society of America
Review question	Should a clinical prediction rule for prognosis plus clinical judgment versus clinical judgment alone be used to determine inpatient versus outpatient treatment location for adults with CAP? This was one of 16 questions addressed in the article, it was the only one relevant to the current review.
Inclusion criteria	Not reported (although focus was on studies that used radiographic criteria for the definition of CAP, US adult patients without immunocompromising conditions such as inherited or acquired immune deficiency or drug-induced neutropenia)
Exclusion criteria	Not reported
Study design of included studies	Two randomised controlled trials and five observational studies
Sample size	Seven included studies, the number of included patients was not reported
Quality of included studies	The quality of the evidence for each outcome of interest was assessed using the GRADE approach, categorised into 4 levels: high, moderate, low and very low. For the two randomised controlled trials the level of certainty was low to moderate. For the five observational studies the quality of evidence was very low for all outcomes.
Target condition/ outcome	30-day mortality, outpatient treatment, subsequent hospitalisation/hospital readmission, ICU admission, hospital length of stay
Patient characteristics	Not reported
Signs, symptoms and early warning scores	PSI and CURB-65
Comparator/ reference standard	Not applicable
Results	Two multicentre, cluster-randomised trials demonstrated that use of the PSI safely increases the proportion of patients who can be treated in the outpatient

	setting. These trials support the safety of using the PSI to guide the initial site of treatment of patients without worsening mortality or other clinically relevant outcomes. Consistent evidence from three pre-post intervention studies and one prospective controlled observational study support the effectiveness and safety of using the PSI to guide the initial site of treatment. In comparison to the PSI, there is less evidence that CURB-65 is effective as a decision aid in guiding the initial site of treatment. One pre-post, controlled intervention study using an electronically calculated version of CURB-65, Pa_{O2}/F_{IO2} <300, absence of pleural effusion, and fewer than three minor ATS severity criteria observed no significant increase in the use of outpatient treatment for adults with CAP.
Authors' conclusion	In addition to clinical judgement, we recommend that clinicians use a validated clinical prediction rule for prognosis, preferentially the Pneumonia Severity Index (PSI) (strong recommendation, moderate quality of evidence) over the CURB-65 (tool based on confusion, urea level, respiratory rate, blood pressure, and age ≥65) (conditional recommendation, low quality of evidence), to determine the need for hospitalisation in adults diagnosed with CAP.
Limitations	This was a poorly reported systematic review, addressing multiple questions including the one of interest here. It is unclear whether all relevant studies were identified and limited details of the included studies were presented.
Comments	There was a high risk of bias for each ROBIS domain. The authors' conclusions appear appropriate based on the studies described, however, in view of the considerable risk of bias, they may not be reliable.

Critical appraisal – ROBIS tool

Overall risk of bias	High (poorly reported review, it is unclear whether all relevant studies were identified and limited details of included studies were presented)
Applicability as a source of data	Acceptable (guideline assessing multiple questions, the question on use of a clinical prediction rule plus clinical judgement versus clinical judgement alone was relevant to this review)

Nannan Panday, 2017

Bibliographic Reference	Nannan Panday RS, Minderhoud TC, Alam N and Nanayakkara PWB. Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): A narrative review. Eur J Intern Med 2017; 45:20-31

Study details

Study type	Systematic review
Study location	Included studies were from Denmark, Netherlands, Norway, Germany, Hong Kong, Ireland, Israel, Italy, Singapore, South Africa, South Korea, Sri Lanka, Sweden, Switzerland, Turkey, UK, USA and Vietnam
Study setting	Emergency department (ED) and Acute Medical Unit (AMU)
Study dates	PubMed and EMBASE were searched from inception to April 2017; included studies were published between 2003 and 2017
Sources of funding	Not reported
Review question	To provide an overview of studies conducted on the value of EWS on predicting intensive care (ICU) admission and mortality in the ED and AMU
Inclusion criteria	Retrospective or prospective observational studies including patients (16 years and older) at the ED or AMU that used the predictive value of EWS as a primary or secondary outcome and the predictive value of the EWS was studied for mortality, intensive care admission or a composite outcome of these
Exclusion criteria	Studies conducted exclusively on patients from disciplines other than internal medicine, where it was unclear when the first assessment of EWS was performed or when the first assessment of EWS was done after the ED or AMU were excluded. Studies where the aim of the study was to determine whether implementation of an EWS led to an improvement in patient mortality and/or ICU admission were also excluded.
Study design of included studies	24 prospective studies and 18 retrospective studies were included; four studies were relevant to this review, one prospective study and 3 retrospective
Sample size	42 included studies, comprising 166,344 patients (range 125 to 39,992). The four studies of relevance to this review comprised of 3,951 patients (range 246 to 2361)
Quality of included studies	Study quality was assessed with the Quality in Prognostic Studies (QUIPS) tool. According to this tool 18 studies were found to have a low risk of bias and were of high quality, 22 studies had a moderate risk of bias and were of moderate quality and 2 studies had a high risk of bias and were of low quality. The subdomains that were most at risk of high bias were study attrition (n = 9) mainly due to inadequate reporting of data on patient follow-up and study confounding due to incomplete reporting on (possible) confounders (n = 14). Of the four studies of relevance to this review, 3 had a low risk of bias and 1 had a moderate risk.
Target condition/ outcome	Mortality, ICU admission, or a composite of these

Patient characteristics	Where reported, mean/median age ranged from 43 to 75. For the 4 studies relevant to our question, median age ranged from 70.5 to 74.
Signs, symptoms and early warning scores	A total of 25 different types of EWS were identified. The most frequently used prognostic scores were the Modified Early Warning Score (MEWS), which was applied in 19 studies, and the National Early Warning Score (NEWS), which was used in 12 studies. Nine studies used the Rapid Emergency Medicine Score (REMS) and seven studied Mortality in the Emergency Department Sepsis score (MEDS). Several variations of the EWS were used, with slight modifications such as adding age, adding laboratory values or different cut-off values. For the 4 studies relevant to our question, the scores assessed were Chronic Respiratory Early Warning Score (CREWS), CRB-65, CURB-65, NEWS, PSI, Systemic Inflammatory Response Syndrome (SIRS), Standardised Early Warning Score (SEWS) and Salford National Early Warning Score (S-NEWS).
Comparator/ reference standard	Not applicable
Results	Due to the heterogeneity of the included studies, results were presented in three groups: studies that included the general ED population, studies that only included patients with a possible infection or sepsis and studies that specifically included patients who had either community acquired pneumonia or respiratory distress. The final group is the one of relevance to this review. Four studies were conducted in the subgroup of patients with community acquired pneumonia or respiratory distress, presenting results as area under the receiver operator characteristic (AUROC). <u>30-day mortality</u> 1 study, 419 ED patients with suspected CAP: AUROC CURB-65: 0.78 AUROC CRB-65: 0.73 AUROC SIRS: 0.68 AUROC SEWS 0.64 1 study, 925 ED patients with suspected CAP: AUROC NEWS: 0.65 AUROC PSI: 0.80 AUROC CURB-65: 0.72 <u>In-hospital mortality</u> 1 study, 2361 ED patients with suspected exacerbation of chronic obstructive pulmonary disease (COPD): AUROC NEWS: 0.74 AUROC CREWS: 0.62 AUROC S-NEWS: 0.62 <u>90-day mortality</u> 1 study, 246 ED patients with respiratory distress: AUROC NEWS: 0.809 <u>ICU admission</u>

	1 study, 925 ED patients with suspected CAP: AUROC NEWS: 0.73 AUROC PSI: 0.64 AUROC CURB-65: 0.64
Authors' conclusion	MEWS and NEWS generally had favourable results in the ED and AMU for all endpoints. For mortality prediction NEWS was the most accurate score in those with respiratory distress. ICU admission was best predicted with NEWS. Many studies have been performed on ED and AMU populations using heterogeneous prognostic scores. However, future studies should concentrate on a simple and easy to use prognostic score such as NEWS with the aim of introducing this throughout the (pre-hospital and hospital) acute care chain.
Limitations	Patients' characteristics (with the exception of age) were not reported and individual study details included in the review were limited so it is not clear how directly relevant the populations of included studies were
Comments	There was a low risk of bias for three ROBIS domains (the other was unclear). The conclusions of the review appear to be appropriate.

Critical appraisal – ROBIS tool

Overall risk of bias	Low
Applicability as a source of data	Acceptable (only a subset of studies was relevant to our review question [patients with suspected CAP or respiratory distress], however one of these studies included patients with suspected exacerbation of COPD)

Smith, 2021

Bibliographic Reference	American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Community-Acquired Pneumonia; Smith MD, Fee C, Mace SE, Maughan B, Perkins JC Jr, Kaji A, Wolf SJ. Clinical Policy: Critical Issues in the Management of Adult Patients Presenting to the Emergency Department With Community-Acquired Pneumonia. Ann Emerg Med 2021; 77(1):e1-e57

Study details

Study type	Systematic review
Study location	Where reported, included studies were from USA, Spain, Switzerland, Australia, Canada, China, France, Japan, Korea, Turkey, UK and Europe
Study setting	Emergency department (ED)
Study dates	Medline, Medline InProcess, Scopus, EMBASE, Web of Science and the Cochrane database were searched between January 2007 and August 30, 2017. Included studies were published between 1997 and 2018.
Sources of funding	American College of Emergency Physicians
Review question	The systematic review addressed a number of questions to inform a revision of the American College of Emergency Physicians Clinical Policy for the management of adult patients presenting to the ED with CAP. The question of relevance to this review is: In the adult ED patient diagnosed with community acquired pneumonia, what clinical decision aids can inform the determination of patient disposition?
Inclusion criteria	No inclusion criteria were listed for the review question, the guideline inclusion criteria were adult ED patients with CAP
Exclusion criteria	No exclusion criteria were listed for the review question, the guideline exclusion criteria were paediatric or pregnant patients
Study design of included studies	Randomised and non-randomised trials, systematic review and meta-analysis, cohort studies (retrospective and prospective, single and multi-centre), observational studies
Sample size	38 studies were included, sample sizes are not reported in the text, but patient numbers are provided in the tables for some studies
Quality of included studies	Each article was assessed, graded and assigned a Class of evidence (Class I, Class II, Class III or Class X (for fatal flaws)) using a predetermined process combining the study's design, methodological quality, and applicability to the critical question. Out of the 38 articles included to answer research question 1, 2 were graded as Class II and 36 were graded as Class III.
Target condition/ outcome	Mortality and ICU admission
Patient characteristics	Not reported

Signs, symptoms and early warning scores	Seven clinical decision aids were identified. Two clinical decision aids to predict mortality in patients with CAP: PSI and CURB-65. Five clinical decision aids to predict the need for ICU admission: Criteria from the American Thoracic Society (ATS) 2001 CAP guidelines; criteria from the 2007 Infectious Diseases Society of America (IDSA)/ATS 2007 CAP guidelines; Severe CAP (SCAP) aid also known as CURXO-80; SMART-COP scale; and Risk of early admission to the ICU (REA-ICU).
Comparator/ reference standard	Not applicable
Results	The authors summarise the findings from the included studies and provide recommendations based on their findings: <u>30-day mortality</u> PSI (7 patient cohorts from 5 class III studies): Risk classes I and II, 30-day mortality rates range 0% to 0.4% and 0.4% to 1.0%, respectively Risk class III, range 0.9% to 3.8 Risk classes IV and V, range 6.0% to 11.4% and 16.8% to 38.3%, respectively CURB-65 (5 patient cohorts from 4 class III studies): Scores of 0 and 1, 30-day mortality rates range 0% to 0.7% and 0% to 3%, respectively Score of 2, range 5.9% to 9.2% Scores of 3, 4, or 5, range 13% to 21.4%, 17% to 41.9%, and 14% to 60%, respectively (There are several variations on the CURB-65, but there are insufficient data to recommend these modified decision aids) Comparison of PSI and CURB-65 for prediction of mortality: Several investigations have compared the performance of PSI and CURB-65. Both the PSI and CURB-65 are appropriate aids for predicting CAP mortality in ED patients. The PSI appears to have slightly greater predictive value for identifying low-risk patients, but this may be offset by the greater number of laboratory studies and longer time needed to complete the PSI compared with the CURB-65. <u>ICU admission:</u> Several prospective trials and systematic reviews have examined the performance of these ICU-specific aids in relation to the PSI and CURB-65. In general, these studies support the use of aids designed to predict ICU admission, such as the 2007 IDSA/ATS minor criteria to identify patients who may benefit from ICU care, rather than relying on mortality-prediction models such as the PSI or CURB-65. However, no studies have prospectively examined the effectiveness or safety of using these ICU admission decision aids to guide patient management.
Author's conclusion	The PSI and CURB-65 are both well-validated clinical decision aids that can predict short-term mortality in patients with CAP and can be used to identity low-risk patients for whom outpatient management may be considered. Both aids are appropriate for this purpose in the emergency care setting; the PSI appears to be slightly better at identifying low-risk patients, but it requires data

	from a greater number of tests, including some not routinely conducted in the ED (i.e., arterial blood gases). For decisions regarding ICU admission, clinical decision aids designed for this purpose (such as the IDSA/ATS minor criteria) should be considered superior to the PSI and CURB-65.
Limitations	Patient characteristics were not reported and differences between the studies were not explored. The authors acknowledge the lack of evidence in some areas requiring consensus recommendations.
Comments	Risk of bias was low or unclear for each ROBIS domain (as insufficient methodological detail is reported in the article). However, the conclusions of the review appear to be appropriate, although it should be noted that some of the authors' conclusions include consensus recommendations as part of the guideline which are not based on the included evidence.

Critical appraisal – ROBIS tool

Overall risk of bias	Unclear
Applicability as a source of data	Good

Appendix E – Early warning scores assessed

Abbreviation/EWS name	Data Required	Range
Centor Cough, Exudate, Nodes Temperature, young OR old modifier	History of fever, tonsillar exudate, anterior cervical lymphadenopathy, absence of cough, age	-1 – 5
CRB-65 Confusion, Respiratory rate, Blood pressure, Age≥65	Mental status, respiratory rate, blood pressure, age ≥65	0 – 4
CREWS Chronic Respiratory Early Warning Score	Pulse, respiratory rate, temperature, blood pressure, spO2, oxygen supplemental, AVPU	0 – 20
CURB-65 Confusion, Urea, Respiratory Rate, Blood pressure, Age≥65	Mental status, urea, respiratory rate, blood pressure, age ≥65	0 – 5
IDSA/ATS 2007 Infectious Diseases Society of America/American Thoracic Society 2007 guidelines	Minor criteria include: respiratory rate, PaO2/FiO2 ratio, multilobar infiltrates, confusion/disorientation, uraemia, leukopenia, thrombocytopenia, hypothermia, hypotension Major criteria include: septic shock with need for vasopressors, respiratory failure requiring mechanical ventilation	Either one major criterion or three or more of the minor criteria
MEDS Mortality in Emergency Department Sepsis	Functional status, vital parameters, lab values	0 – 27
MEWS Modified Early Warning Score	Pulse, respiratory rate, temperature, urinary output, blood pressure, AVPU	0 – 17
NEWS National Early Warning Score	Pulse, respiratory rate, temperature, blood pressure, spO2, oxygen supplemental, AVPU	0 – 20
PSI Pneumonia Severity Index	Age, type of residence, laboratory values, vital parameters	0 – 395
REA-ICU Risk of Early Admission to the ICU	Male gender, age <80, comorbid conditions, respiratory rate, heart rate, multilobar infiltrate or pleural effusion, white blood cell count, hypoxaemia, blood urea nitrogen, arterial pH, sodium	0 – 17
REMS Rapid Emergency Medicine Score	Age, blood pressure, heart rate, respiratory rate, spO2, GCS	0 – 26
SCAP Severe CAP Also known as CURXO-80 Confusion, Urea, Respiratory rate, X-ray multilobar bilateral, Oxygenation, age≥80	Minor criteria include: confusion, urea, respiratory rate, multilobar involvement, oxygenation, age ≥80 Major criteria include: arterial pH, systolic blood pressure	Either one major criterion or two or more minor criteria
SEWS Standardised Early Warning Score	Pulse, respiratory rate, temperature, blood pressure, spO2, AVPU	0 – 18
SIRS Systemic Inflammatory Response Syndrome	Vital parameters + lab values	0 – 4
SMART-COP Systolic blood pressure, Multilobar chest radiography	Blood pressure, multilobar involvement, albumin level, respiratory rate, tachycardia, confusion, oxygenation, arterial pH	0 – 11

involvement, Albumin level, Respiratory rate, Tachycardia, Confusion, Oxygenation, and arterial pH		
S-NEWS Salford National Early Warning Score	Pulse, respiratory rate, temperature, blood pressure, spO2, oxygen supplemental, AVPU	0 – 20

Abbreviations: AVPU = Alert, Verbally responsive, Painfully responsive, Unresponsive; GCS = Glasgow Coma Scale; PaO2/FiO2 ratio = ratio of arterial oxygen partial pressure to fractional inspired oxygen; SpO2 = oxygen saturation.

Note: None of the reviews assessed NEWS2; NEWS was updated to NEWS2 in December 2017.

Appendix F – Forest plots

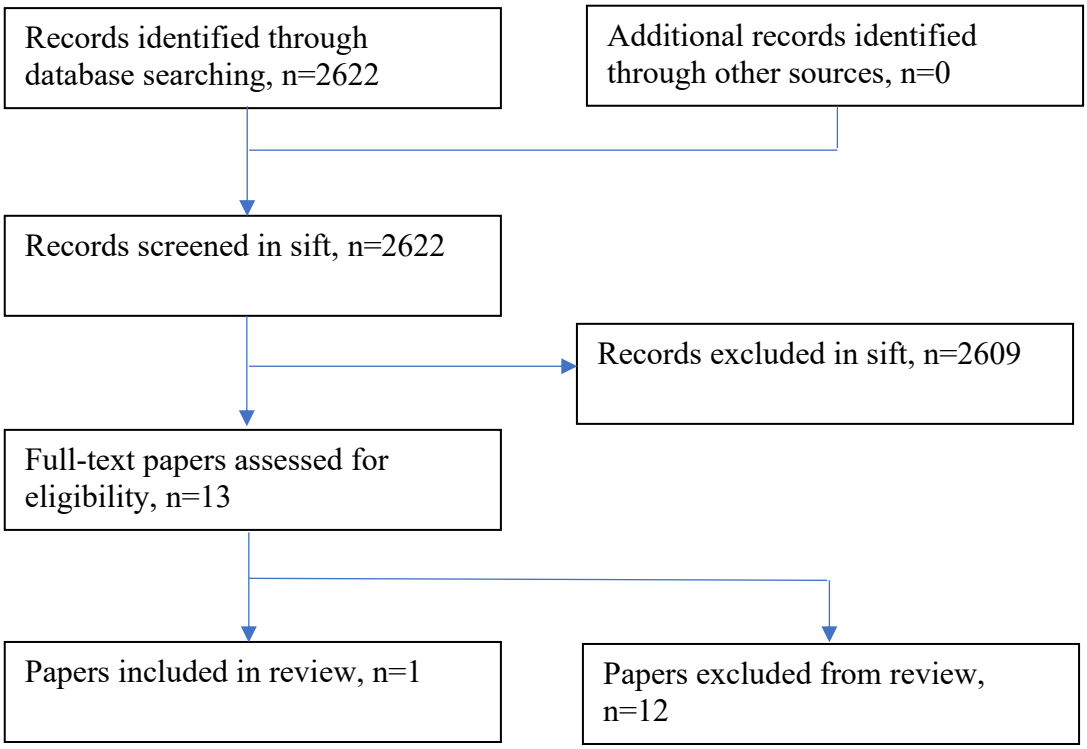
Not applicable.

Appendix G – ROBIS risk of bias assessment results

Review	Phase 2 risk of bias				Phase 3
	1. Study eligibility criteria	2. Identification and selection of studies	3. Data collection and study appraisal	4. Synthesis and findings	Risk of bias in the review
Aalbers (2011)[2]	Low	Low	Low	Low	Low
Akram (2011)[3]	Low	Low	Low	Low	Low
Chalmers (2011)[4]	Low	Low	Low	Low	Low
Dosa (2005)[10]	High	High	High	High	High
Ebell (2019)[5]	Low	High	Low	Low	Low
McNally (2010)[6]	Low	Low	Low	Low	Low
Metlay (2019)[7]	High	High	High	High	High
Nannan Panday (2017)[8]	Low	Low	Unclear	Low	Low
Smith (2021)[9]	Unclear	Low	Unclear	Unclear	Unclear

Appendix H – Economic evidence study selection

Figure 2: Flow chart of economic study selection for the review of signs, symptoms and early warning scores for predicting severe illness in the initial assessment of people aged 16 years or over with suspected acute respiratory infection



Appendix I – Economic evidence tables

Table 7: Economic evidence

Study details	Population and setting	Interventions and comparators	Outcomes and methods of analysis	Results	Sensitivity analyses	Additional comments
Little (2014)[12] Trial-based cost-utility and cost-effectiveness study	Patients aged ≥ 3 years with acute sore throat symptoms Primary care (UK) NHS & PSS perspective	Clinical symptom scores and rapid antigen detection tests (RADTs) vs delayed antibiotics	Outcomes: Symptom severity score and quality-adjusted life year (QALY) QALYs were estimated using EQ5D scores obtained from a 14-day patient diary Costs included: GP/NP visit (based on PSSRU (2011)), testing costs (obtained from manufacturer), prescribing fees (based on the NHS	Cost-effectiveness: The clinical score group dominated RADT and delayed prescribing at a cost per point change (95% CI) of £44.20 (41.30 to 47.00), £49.30 (46.00 to 52.50) and £51.30 (43.30 to 59.20), respectively. Cost-utility: QALY gain was marginally higher in the RADT group compared to the symptom severity score group with ICERs of £74,286 and £24,528 using adjusted QALY data	CEACs show considerable uncertainty around the QALY estimate in cost-utility results. The probabilities that delayed prescribing, clinical score and RADT are cost-effective were 25%, 40% and 35% respectively, for the 14-day period, and 28%, 38% and 35%, respectively, for the 28-day period.	Source of funding: National Institute for Health Research (NIHR), Health Technology Assessment (HTA) commissioned The authors noted some limitations, including that the 14-day diary had EQ5D data was available for 52% of all participants and was collected at only two time points (0 and 14 days). There were no statistically significant differences in QALYs between the three groups. A reason for this may be that the

Study details	Population and setting	Interventions and comparators	Outcomes and methods of analysis	Results	Sensitivity analyses	Additional comments
			drug tariff) and drug costs (obtained from the BNF). Community care contacts from illness or treatment complications were also included and costed using PSSRU and NHS reference costs. 28-day time horizon No discounting applied due to the short time horizon	for the 14-day and 28-day period, respectively. Delayed prescribing was dominated over both periods.		QALY difference at 14 days was not well correlated with changes in symptom severity. This analysis demonstrated the potential cost-effectiveness of using clinical scores in managing symptoms for sore throat.

Table 8: Economic evaluation quality checklist

Study identification **Little P, Hobbs FD, Moore M, Mant D, Williamson I, McNulty C, et al. PRImary care Streptococcal Management (PRISM) study: in vitro study, diagnostic cohorts and a pragmatic adaptive randomised controlled trial with nested qualitative study and cost-effectiveness study. Health Technol Assess. 2014;18(6): 1-101**		
Category	**Rating**	**Comments**
Applicability		
1.1 Is the study population appropriate for the review question?	No	Not directly applicable to the review question, however this study met the inclusion criteria.
1.2 Are the interventions appropriate for the review question?	Partly	Clinical symptom scores are assessed.
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	
1.4 Is the perspective for costs appropriate for the review question?	Yes	NHS and PSS perspective.
1.5 Is the perspective for outcomes appropriate for the review question?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	N/A	Due to short time horizon. The analysis covered a 28-day follow-up period.
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.5 above).	Yes	QALYs were derived from EQ5D scores.
1.8 OVERALL JUDGEMENT	**PARTIALLY APPLICABLE**	
Other comments:		
Study limitations		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	N/A	Trial-based analysis.
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Yes	

Study identification **Little P, Hobbs FD, Moore M, Mant D, Williamson I, McNulty C, et al. PRImary care Streptococcal Management (PRISM) study: in vitro study, diagnostic cohorts and a pragmatic adaptive randomised controlled trial with nested qualitative study and cost-effectiveness study. Health Technol Assess. 2014;18(6): 1-101**		
Category	**Rating**	**Comments**
2.8 Are the unit costs of resources from the best available source?	Yes	
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11 Has no potential financial conflict of interest been declared?	Yes	
2.12 OVERALL ASSESSMENT	**MINOR LIMITATIONS**	

Appendix J – Health economic model

No original economic modelling was undertaken for this review.

Appendix K – Excluded studies

Table 9: Studies excluded from the clinical review

Study	Exclusion reason
Al Hussain S K, Kurdi A, Abutheraa N et al. 2021. "Validity of Pneumonia Severity Assessment Scores in Africa and South Asia: A Systematic Review and Meta-Analysis". *Healthcare* 9:11	Population (includes hospitalised patients)
Anevlavis S and Bouros D. 2010. "Community acquired bacterial pneumonia". *Expert Opinion on Pharmacotherapy* 11:361-74	Study design (not a systematic review)
Anonymous. 2022. "Age-sex differences in the global burden of lower respiratory infections and risk factors, 1990-2019: results from the Global Burden of Disease Study 2019". *The Lancet Infectious Diseases* 22:1626-1647	Study design (not a systematic review)
Asrar Khan W and Woodhead M. 2013. "Major advances in managing community-acquired pneumonia". *F1000Prime Reports* 5:43	Study design (not a systematic review)
Barbagelata E, Cilloniz C, Dominedo C et al. 2020. "Gender differences in community-acquired pneumonia". *Minerva Medica* 111:153-165	Population (includes children and hospitalised patients)
Bergmann M, Haasenritter J, Beidatsch D et al. 2021. "Prevalence, aetiologies and prognosis of the symptom cough in primary care: a systematic review and meta-analysis". *BMC Family Practice* 22:151	Intervention (assesses prevalence, aetiologies and prognosis, not symptoms, signs and EWS)
Berti E, Galli L, de Martino M and Chiappini E. 2013. "International guidelines on tackling community-acquired pneumonia show major discrepancies between developed and developing countries". *Acta Paediatrica* 102:4-16	Population (includes children)
Bird J H, Biggs T C and King E V. 2014. "Controversies in the management of acute tonsillitis: an evidence-based review". *Clinical Otolaryngology* 39:368-74	Study design (not a systematic review)
Boulet L P. 2006. "Future directions in the clinical management of cough: ACCP evidence-based clinical practice guidelines". *Chest* 129:287S-292S	Study design (not a systematic review)
Braman S S. 2006. "Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines". *Chest* 129:95S-103S	Study design (not a systematic review)
Bryan C and Boren S A. 2008. "The use and effectiveness of electronic clinical decision support tools in the ambulatory/primary care setting: A systematic review of the	Population (not specific to ARI)

literature". *Informatics in Primary Care* 16(2):79-91	
Cabanas A M, Fuentes-Guajardo M, Latorre K et al. 2022. "Skin Pigmentation Influence on Pulse Oximetry Accuracy: A Systematic Review and Bibliometric Analysis". *Sensors* 22:29	Population (includes ICU patients, healthy adults, children and COVID patients)
Caini S, Kroneman M, Wiegers T et al. 2018. "Clinical characteristics and severity of influenza infections by virus type, subtype, and lineage: A systematic literature review". *Influenza & Other Respiratory Viruses* 12:780-792	Population (includes children and hospitalised patients)
Campbell S G, Patrick W, Urquhart D G et al. 2004. "Patients with community acquired pneumonia discharged from the emergency department according to a clinical practice guideline". *Emergency Medicine Journal* 21:667-9	Study design (not a systematic review)
Carvalho E, Estrela M, Zapata-Cachafeiro M et al. 2020. "E-Health Tools to Improve Antibiotic Use and Resistances: A Systematic Review". *Antibiotics* 9:12	Population (includes children and hospitalised patients)
Chalmers J D, Singanayagam A, Akram A R et al. 2010. "Severity assessment tools for predicting mortality in hospitalised patients with community-acquired pneumonia. Systematic review and meta-analysis". *Thorax* 65:878-83	Population (includes hospitalised patients)
Chalmers J D, Mandal P, Singanayagam A et al. 2011. "Severity assessment tools to guide ICU admission in community-acquired pneumonia: systematic review and meta-analysis". *Intensive Care Medicine* 37:1409-20	Population (includes hospitalised patients)
Chalmers J D and Rutherford J. 2012. "Can we use severity assessment tools to increase outpatient management of community-acquired pneumonia?". *European Journal of Internal Medicine* 23(5):398-406	Study design (not a systematic review)
Chen G, Xu K, Sun F et al. 2020. "Risk Factors of Multidrug-Resistant Bacteria in Lower Respiratory Tract Infections: A Systematic Review and Meta-Analysis". *The Canadian Journal of Infectious Diseases & Medical Microbiology* 2020:7268519	Population (includes children and hospitalised patients)
Chiappini E, Regoli M, Bonsignori F et al. 2011. "Analysis of different recommendations from international guidelines for the management of acute pharyngitis in adults and children". *Clinical Therapeutics* 33:48-58	Outcomes (compares international guidelines on the management of pharyngitis, does not report relevant outcomes)
Cho I and Bates D W. 2018. "Behavioral Economics Interventions in Clinical Decision Support Systems". *Yearbook of Medical Informatics* 27:114-121	Intervention (background paper on clinical decision support systems, not signs, symptoms and EWS)

Cohen Jf, Pauchard J-Y, Hjelm N et al. 2020. "Efficacy and safety of rapid tests to guide antibiotic prescriptions for sore throat". *Cochrane Database of Systematic Reviews* 6	Population (includes children)
Corrales-Medina V F, Suh K N, Rose G et al. 2011. "Cardiac complications in patients with community-acquired pneumonia: a systematic review and meta-analysis of observational studies". *PLoS Medicine / Public Library of Science* 8:e1001048	Population (includes hospitalised patients)
Correa R A, Costa A N, Lundgren F et al. 2018. "2018 recommendations for the management of community acquired pneumonia". *Jornal Brasileiro De Pneumologia: Publicacao Oficial Da Sociedade Brasileira De Pneumologia E Tisilogia* 44:405-423	Study design (not a systematic review)
Coutinho G, Duerden M, Sessa A et al. 2021. "Worldwide comparison of treatment guidelines for sore throat". *International Journal of Clinical Practice* 75(5) (no pagination)	Outcomes (comparison of guidelines, no outcomes of interest)
Dale A P, Marchello C and Ebell M H. 2019. "Clinical gestalt to diagnose pneumonia, sinusitis, and pharyngitis: a meta-analysis". *British Journal of General Practice* 69:e444-e453	Intervention (assessment of clinical gestalt rather than signs and symptoms)
DeLaney M and Khoury C. 2021. "Community-acquired pneumonia in the emergency department". *Emergency Medicine Practice* 23:1-24	Study design (not a systematic review)
Demirdal T, Sen P and Emir B. 2021. "Predictors of mortality in invasive pneumococcal disease: a meta-analysis". *Expert Review of Antiinfective Therapy* 19:927-944	Population (includes children and non-ARI patients)
Derber C J and Troy S B. 2012. "Head and neck emergencies: bacterial meningitis, encephalitis, brain abscess, upper airway obstruction, and jugular septic thrombophlebitis". *Medical Clinics of North America* 96:1107-26	Study design (not a systematic review)
Dhawan N, Pandya N, Khalili M et al. 2015. "Predictors of mortality for nursing home-acquired pneumonia: a systematic review". *BioMed Research International* 2015:285983	Outcomes (unclear whether relevant outcomes are assessed within 4 weeks of consultation; outcomes/results are discussed, rather than clearly reported)
Dobler C C, Sanchez M, Gionfriddo M R et al. 2019. "Impact of decision aids used during clinical encounters on clinician outcomes and consultation length: a systematic review". *BMJ Quality & Safety* 28:499-510	Intervention (clinical decision rules for a range of conditions, not just ARI)
Dosa D. 2006. "Should I hospitalize my resident with nursing home-acquired	Duplicate report

pneumonia?". *Journal of the American Medical Directors Association* 7:S74-80, 73	
Durand C, Alfandari S, Beraud G et al. 2022. "Clinical Decision Support Systems for Antibiotic Prescribing: An Inventory of Current French Language Tools". *Antibiotics* 11:14	Population (includes children and non-ARI conditions)
Ebell M H, Smith M A, Barry H C et al. 2000. "The rational clinical examination. Does this patient have strep throat?". *JAMA* 284:2912-8	Study design (not a systematic review)
Ebell M H, White L L and Casault T. 2004. "A systematic review of the history and physical examination to diagnose influenza". *Journal of the American Board of Family Practice* 17:1-5	Outcomes (outcome was confirmed diagnosis of influenza, no outcomes relating to severity of disease, etc)
Ebell M H and Afonso A. 2011. "A systematic review of clinical decision rules for the diagnosis of influenza". *Annals of Family Medicine* 9:69-77	Outcomes (outcome was confirmed diagnosis of influenza, no outcomes relating to severity of disease, etc)
Ebell M H and Grad R. 2015. "Top 20 Research Studies of 2014 for Primary Care Physicians". *American Family Physician* 92:377-83	Intervention
Ebell M H, Marchello C and Callahan M. 2017. "Clinical Diagnosis of Bordetella Pertussis Infection: A Systematic Review". *Journal of the American Board of Family Medicine: JABFM* 30:308-319	Outcomes (outcome was confirmed diagnosis of Bordetella Pertussis Infection, no outcomes relating to severity of disease, etc)
Ebell M H, McKay B, Dale A et al. 2019. "Accuracy of Signs and Symptoms for the Diagnosis of Acute Rhinosinusitis and Acute Bacterial Rhinosinusitis". *Annals of Family Medicine* 17:164-172	Outcomes (outcome was confirmed diagnosis of acute rhinosinusitis and acute bacterial rhinosinusitis, no outcomes relating to severity of disease, etc)
Ebell M H, Rahmatullah I, Cai X et al. 2021. "A Systematic Review of Clinical Prediction Rules for the Diagnosis of Influenza". *Journal of the American Board of Family Medicine: JABFM* 34:1123-1140	Population (includes children)
El-Gohary M, Hay A D, Coventry P et al. 2013. "Corticosteroids for acute and subacute cough following respiratory tract infection: a systematic review". *Family Practice* 30:492-500	Intervention (treatment, not assessment of severity)
Elmenawi K A, Anil V, Gosal H et al. 2021. "The Importance of Measuring Troponin in Chronic Obstructive Pulmonary Disease Exacerbations: A Systematic Review". *Cureus* 13:e17451	Population (exacerbation of COPD, not suspected ARI patients)
Exarchos K P, Aggelopoulou A, Oikonomou A et al. 2022. "Review of Artificial Intelligence Techniques in Chronic Obstructive Lung Disease". *IEEE Journal of Biomedical and Health Informatics* 26(5):2331-2338	Population (COPD, not suspected ARI patients)

Fall A, Kenmoe S, Ebogo-Belobo J T et al. 2022. "Global prevalence and case fatality rate of Enterovirus D68 infections, a systematic review and meta-analysis". *PLoS Neglected Tropical Diseases [electronic resource]* 16:e0010073	Intervention (prevalence and case fatality rate, not assessment of signs and symptoms)
Fendrick A M, Saint S, Brook I et al. 2001. "Diagnosis and treatment of upper respiratory tract infections in the primary care setting". *Clinical Therapeutics* 23:1683-706	Study design (not a systematic review)
Ferdinands J M, Thompson M G, Blanton L et al. 2021. "Does influenza vaccination attenuate the severity of breakthrough infections? A narrative review and recommendations for further research". *Vaccine* 39:3678-3695	Population (includes hospitalised patients and children)
Fischer C, Knusli J, Lhopitallier L et al. 2023. "Pulse Oximetry as an Aid to Rule Out Pneumonia among Patients with a Lower Respiratory Tract Infection in Primary Care". *Antibiotics* 12:02	Study design (not a systematic review)
Franciosi L G, Page C P, Celli B R et al. 2006. "Markers of exacerbation severity in chronic obstructive pulmonary disease". *Respiratory Research* 7:74	Population (COPD not ARI)
Froom J, Culpepper L, Green L A et al. 2001. "A cross-national study of acute otitis media: risk factors, severity, and treatment at initial visit. Report from the International Primary Care Network (IPCN) and the Ambulatory Sentinel Practice Network (ASPN)". *Journal of the American Board of Family Practice* 14:406-17	Population (includes children)
Garten S and Falkner R V. 2003. "Continual smoking of mentholated cigarettes may mask the early warning symptoms of respiratory disease". *Preventive Medicine* 37(4):291-296	Study design (not a systematic review)
Gleeson L L, Clyne B, Barlow J W et al. 2022. "Medication safety incidents associated with the remote delivery of primary care: a rapid review". *International Journal of Pharmacy Practice* 30:495-506	Intervention (not related to ARI)
Goka E A, Vallely P J, Mutton K J and Klapper P E. 2014. "Single and multiple respiratory virus infections and severity of respiratory disease: a systematic review". *Paediatric Respiratory Reviews* 15:363-7	Population (includes hospitalised patients and children)
Graffelman A W, le Cessie S, Knuistingh Neven A et al. 2007. "Can history and exam alone reliably predict pneumonia?". *Journal of Family Practice* 56:465-70	Study design (not a systematic review)
Haimi M and Gesser-Edelsburg A. 2022. "Application and implementation of telehealth services designed for the elderly population during the COVID-19 pandemic: A systematic	Intervention (telemedicine services, not assessment of ARI)

review". *Health Informatics Journal* 28:14604582221075561	
Hirner S, Pigoga J L, Naidoo A V et al. 2021. "Potential solutions for screening, triage, and severity scoring of suspected COVID-19 positive patients in low-resource settings: a scoping review". *BMJ Open* 11:e046130	Intervention (focused on patients suspected or confirmed COVID, not ARI)
Htun TP, Sun Y, Chua H L and Pang J. Clinical features for diagnosis of pneumonia among adults in primary are setting: A systematic and meta-review. Scientific Reports 2019; 9:7600	Outcome (outcome is diagnosis of pneumonia, not escalation of care, antibiotic use, severity, mortality, etc)
Huntley A L, Davies B, Jones N et al. 2020. "Determining when a hospital admission of an older person can be avoided in a subacute setting: a systematic review and concept analysis". *Journal of Health Services & Research Policy* 25:252-264	Intervention (not assessment of scoring methods or procedures to assess patients with ARI)
Justicia-Grande A J, Pardo Seco J, Rivero Calle I and Martinon-Torres F. 2017. "Clinical respiratory scales: which one should we use?". *Expert Review of Respiratory Medicine* 11:925-943	Population (includes children and non-ARI)
Kerdemelidis M, Lennon D, Arroll B and Peat B. 2009. "Guidelines for sore throat management in New Zealand". *New Zealand Medical Journal* 122:10-8	Population (includes children)
Kolditz M and Ewig S. 2017. "Community-Acquired Pneumonia in Adults". *Deutsches Arzteblatt International* 114:838-848	Study design (not a systematic review)
Kruger K, Topfner N, Berner R et al. 2021. “Clinical practice guideline: sore throat”. *Deutsches Arzteblatt International* 118:188-94	Population (includes children)
Kruger K, Holzinger F,Trauth J et al. 2022. "Chronic Cough". *Deutsches Arzteblatt International* 119:59-65	Population (chronic cough, not ARI)
Kulik E, Stuart B and Willcox M. 2022. "Predictors of rheumatic fever in sore throat patients: a systematic review and meta-analysis". *Transactions of the Royal Society of Tropical Medicine & Hygiene* 116:286-297	Population (includes children)
Kwok C S, Loke Y K, Woo K and Myint P K. 2013. "Risk prediction models for mortality in community-acquired pneumonia: a systematic review". *BioMed Research International* 2013:504136.	Population (includes hospitalised patients)
Launders N, Ryan D, Winchester C C et al. 2019. "Management Of Community-Acquired Pneumonia: An Observational Study In UK Primary Care". *Pragmatic & Observational Research* 10:53-65	Study design (not a systematic review)
Li J, Zhou K, Duan H et al. 2022. "Value of D-dimer in predicting various clinical outcomes following community-acquired pneumonia: A	Intervention (assessment of D-dimer, not signs, symptoms and EWS)

network meta-analysis". *PLoS ONE [Electronic Resource]* 17:e0263215	
Liapikou A and Torres A. 2013. "Current treatment of community-acquired pneumonia". *Expert Opinion on Pharmacotherapy* 14:1319-32	Intervention (therapies for patients with CAP, not severity or outcomes)
Little P, Rumsby K, Kelly J et al. 2005. "Information leaflet and antibiotic prescribing strategies for acute lower respiratory tract infection: a randomized controlled trial". *JAMA* 293:3029-35	Study design (not a systematic review)
Little P and Williamson I. 1996. "Sore throat management in general practice". *Family Practice* 13:317-21	Intervention (treatment and management, not assessment of symptoms and outcomes)
Loeb M. 2010. "Community-acquired pneumonia". *Clinical Evidence* 18:18	Intervention (therapies for patients with CAP, not assessment of severity)
Loke Y K, Kwok C S, Niruban A and Myint P K. 2010. "Value of severity scales in predicting mortality from community-acquired pneumonia: systematic review and meta-analysis". *Thorax* 65:884-90	Population (includes hospitalised patients)
Long B, Long D and Koyfman A. 2017. "Emergency Medicine Evaluation of Community-Acquired Pneumonia: History, Examination, Imaging and Laboratory Assessment, and Risk Scores". *Journal of Emergency Medicine* 53(5):642-652	Study design (not a systematic review)
Ma H M, Ip M and Woo J. 2015. "Effect of age and residential status on the predictive performance of CURB-65 score". *Internal Medicine Journal* 45(3):300-304	Study design (not a systematic review)
Magaziner J, Tenney J H, DeForge B et al. 1991. "Prevalence and characteristics of nursing home-acquired infections in the aged". *Journal of the American Geriatrics Society* 39:1071-8	Study design (not a systematic review)
Malosh R E, Martin E, Ortiz J R and Monto A S. 2018. "The risk of lower respiratory tract infection following influenza virus infection: A systematic and narrative review". *Vaccine* 36:141-147	Population (includes children)
Marchello C S, Ebell M H, Dale A P et al. 2019. "Signs and Symptoms That Rule out Community-Acquired Pneumonia in Outpatient Adults: A Systematic Review and Meta-Analysis". *Journal of the American Board of Family Medicine: JABFM* 32:234-247	Outcomes (outcome is diagnosis of CAP, not escalation of care, antibiotic use, severity, mortality, etc)
Marti C, Garin N, Grosgurin O et al. 2012. "Prediction of severe community-acquired pneumonia: a systematic review and meta-analysis". *Critical Care (London, England)* 16:R141	Population (includes hospitalised patients)

Martinez F J. 2004. "Acute exacerbations of chronic bronchitis: Diagnosis and therapy". *Journal of Clinical Outcomes Management* 11(10):659-673	Study design (not a systematic review)
Matthys H and Kamin W. 2013. "Positioning of the Bronchitis Severity Score (BSS) for standardised use in clinical studies". *Current Medical Research & Opinion* 29:1383-90	Population (includes children)
Maxwell D J and Easton K L. 2004. "Community-acquired pneumonia". *Journal of Pharmacy Practice and Research* 34(3):212-217	Study design (not a systematic review)
McDonagh M S, Peterson K, Winthrop K et al. 2018. "Interventions to reduce inappropriate prescribing of antibiotics for acute respiratory tract infections: summary and update of a systematic review". *Journal of International Medical Research* 46(8):3337-3357	Intervention (interventions to reduce prescribing, not EWS or signs and symptoms)
Memon R A, Rashid M A, Avva S et al. 2022. "The Use of the SMART-COP Score in Predicting Severity Outcomes Among Patients With Community-Acquired Pneumonia: A Meta-Analysis". *Cureus* 14:e27248	Population (includes hospitalised patients)
Mertz D, Lo C K, Lytvyn L et al. 2019. "Pregnancy as a risk factor for severe influenza infection: an individual participant data meta-analysis". *BMC Infectious Diseases* 19:683	Population (pregnant women, also includes hospitalised patients)
Modi A R and Kovacs C S. 2020. "Community-acquired pneumonia: Strategies for triage and treatment". *Cleveland Clinic Journal of Medicine* 87:145-151	Study design (not a systematic review)
Moore A, Ashdown H F, Shinkins B et al. 2017. "Clinical Characteristics of Pertussis-Associated Cough in Adults and Children: A Diagnostic Systematic Review and Meta-Analysis". *Chest* 152:353-367	Population (includes children and hospitalised patients)
Moore A, Harnden A, Grant C C et al. 2019. "Clinically Diagnosing Pertussis-associated Cough in Adults and Children: CHEST Guideline and Expert Panel Report". *Chest* 155:147-154	Study design (not a systematic review)
Morice A H. 2017. "A new way to look at acute cough in the pharmacy". *Clinical Pharmacist* 9	Study design (not a systematic review)
Moriyama M, Hugentobler W J and Iwasaki A. 2020. "Seasonality of Respiratory Viral Infections". *Annual Review of Virology* 7:83-101	Study design (not a systematic review)
Mosby L G, Rasmussen S A and Jamieson D J. 2011. "2009 pandemic influenza A (H1N1) in pregnancy: a systematic review of the literature". *American Journal of Obstetrics & Gynecology* 205:10-8	Intervention (impact of pandemic H1N1 influenza in pregnancy, not assessment of symptoms, signs and EWS in ARI)
Myint P K, Kwok C S, Majumdar S R et al. 2012. "The International Community-Acquired Pneumonia (CAP) Collaboration Cohort (ICCC)	Population (includes hospitalised patients)

study: rationale, design and description of study cohorts and patients". *BMJ Open* 2	
Nabovati E, Jeddi F R, Farrahi R and Anvari S. 2021. "Information technology interventions to improve antibiotic prescribing for patients with acute respiratory infection: a systematic review". *Clinical Microbiology & Infection* 27:838-845	Intervention (includes children and hospitalised patients)
Neuner J M, Hamel M B, Phillips R S et al. 2003. "Diagnosis and management of adults with pharyngitis. A cost-effectiveness analysis". *Annals of Internal Medicine* 139:113-22	Study design (not a systematic review)
Noguchi S, Yatera K, Kawanami T et al. 2017. "Pneumonia Severity Assessment Tools for Predicting Mortality in Patients with Healthcare-Associated Pneumonia: A Systematic Review and Meta-Analysis". *Respiration* 93:441-450	Population (includes hospitalised patients)
Obisesan O. 2005. "The evaluation of upper respiratory tract infection symptoms to show the significance of developing a quality-of-life evaluation instrument for upper respiratory tract infections to assess respiratory disorder-related disability". *American Journal of Therapeutics* 12:142-50	Study design (not a systematic review)
Petrozzino J J, Smith C and Atkinson M J. 2010. "Rapid diagnostic testing for seasonal influenza: an evidence-based review and comparison with unaided clinical diagnosis". *Journal of Emergency Medicine* 39:476-490.e1	Population (includes children)
Phua J, Dean N C, Guo Q et al. Severe community-acquired pneumonia: timely management measures in the first 24 hours. Critical Care 2016; 20:237	Population (includes hospitalised patients)
Ponnapalli A, Khare Y, Dominic C et al. 2021. "Remote risk-stratification of dyspnoea in acute respiratory disorders: a systematic review of the literature". *Journal of the Royal College of Physicians of Edinburgh* 51:221-229	Population (includes children, hospitalised patients and COVID patients)
Pratter M R. 2006. "Overview of common causes of chronic cough: ACCP evidence-based clinical practice guidelines". *Chest* 129:59S-62S	Population (chronic cough, not ARI)
Renaud B, Santin A, Coma E et al. 2009. "Association between timing of intensive care unit admission and outcomes for emergency department patients with community-acquired pneumonia". *Critical Care Medicine* 37:2867-74	Study design (not a systematic review)
Rodriguez-Acelas A L, Reich R, de Abreu Almeida M et al. 2016. "Nursing outcome "Severity of infection": conceptual definitions for indicators related to respiratory problems". *Investigacion y Educacion en Enfermeria* 34:38-45	Intervention (not an assessment of symptoms, signs and EWS for the assessment of ARI)

Rombauts A, Abelenda-Alonso G, Cuervo G et al. 2022. "Role of the inflammatory response in community-acquired pneumonia: clinical implications". *Expert Review of Antiinfective Therapy* 20:1261-1274	Study design (not a systematic review)
Rottman S J, Shoaf K I, Schlesinger J et al. 2010. "Pandemic influenza triage in the clinical setting". *Prehospital & Disaster Medicine* 25:99-104	Study design (not a systematic review)
Schmit K M, Coeytaux R R, Goode A P et al. 2013. "Evaluating cough assessment tools: a systematic review". *Chest* 144:1819-1826	Population (includes tools for lung cancer, lung transplant, etc, not just ARI)
Schofield C, Colombo R E, Richard S A et al. 2020. "Comparable Disease Severity by Influenza Virus Subtype in the Acute Respiratory Infection Consortium Natural History Study". *Military Medicine* 185:e1008-e1015	Study design (not a systematic review)
Schuetz P, Koller M, Christ-Crain M et al. 2008. "Predicting mortality with pneumonia severity scores: Importance of model recalibration to local settings". *Epidemiology and Infection* 136(12):1628-1637	Study design (not a systematic review)
Simpson S H, Marrie T J and Majumdar S R. 2005. "Do guidelines guide pneumonia practice? A systematic review of interventions and barriers to best practice in the management of community-acquired pneumonia". *Respiratory Care Clinics of North America* 11:1-13	Intervention (adherence to guidelines, not assessment of symptoms, signs and EWS)
Solari L, Acuna-Villaorduna C, Soto A and van der Stuyft P. 2011. "Evaluation of clinical prediction rules for respiratory isolation of inpatients with suspected pulmonary tuberculosis". *Clinical Infectious Diseases* 52:595-603	Population (patients with pulmonary tuberculosis, not ARI)
Solari L, Soto A and Van der Stuyft P. 2017. "Performance of clinical prediction rules for diagnosis of pleural tuberculosis in a high-incidence setting". *Tropical Medicine & International Health* 22:1283-1292	Population (patients with pleural tuberculosis, not ARI)
Song W J, Kim H J, Shim J S et al. 2017. "Diagnostic accuracy of fractional exhaled nitric oxide measurement in predicting cough-variant asthma and eosinophilic bronchitis in adults with chronic cough: A systematic review and meta-analysis". *Journal of Allergy & Clinical Immunology* 140:701-709.	Population (chronic cough not ARI)
Sunjaya A P, Ansari S and Jenkins C R. 2022. "A systematic review on the effectiveness and impact of clinical decision support systems for breathlessness". *npj Primary Care Respiratory Medicine* 32(1) (no pagination)	Population (not ARI)

Thai T N, Dale A P and Ebell M H. 2018. "Signs and symptoms of Group A versus Non-Group A strep throat: A meta-analysis". *Family Practice* 35:231-238	Population (includes children)
Torres A, Chalmers J D, Dela Cruz C S et al. 2019. "Challenges in severe community-acquired pneumonia: a point-of-view review". *Intensive Care Medicine* 45:159-171	Study design (not a systematic review)
Vines C and Dean N C. 2012. "Technology implementation impacting the outcomes of patients with CAP". *Seminars in Respiratory & Critical Care Medicine* 33:292-7	Intervention (assessment of technology implementation, not symptoms, signs and EWS)
Wallace E, Uijen M J, Clyne B et al. Impact analysis studies of clinical prediction rules relevant to primary care: a systematic review. BMJ Open 2016; 6:e009957	Population (includes children)
Willis B H, Coomar D and Baragilly M. 2020. "Comparison of Centor and McIsaac scores in primary care: a meta-analysis over multiple thresholds". *British Journal of General Practice* 70:e245-e254	Population (includes children)
Womack J and Kropa J. 2022. "Community-Acquired Pneumonia in Adults: Rapid Evidence Review". *American Family Physician* 105:625-630	Study design (not a systematic review)
Woolley S L, Bernstein J M, Davidson J A and Smith D R. 2005. "Sore throat in adults--does the introduction of a clinical scoring system improve the management of these patients in a secondary care setting?". *Journal of Laryngology & Otology* 119:550-5	Study design (not a systematic review)
Xie C X, Chen Q, Hincapie C A et al. 2022. "Effectiveness of clinical dashboards as audit and feedback or clinical decision support tools on medication use and test ordering: a systematic review of randomized controlled trials". *Journal of the American Medical Informatics Association* 29:1773-1785	Population (any health condition, not specifically ARI)

Table 10: Studies excluded from the economic review

Study	Exclusion reason(s)
Bartenschlager, C. C., et al. (2022). "A Simulation-Based Cost-Effectiveness Analysis of Severe Acute Respiratory Syndrome Coronavirus 2 Infection Prevention Strategies for Visitors of Healthcare Institutions." VALUE IN HEALTH 25(11): 1846-1852	Intervention (assessment of infection prevention strategies)
Bashir, S., et al. (2022). "Economic analysis of different throughput scenarios and implementation strategies of computer-aided detection software as a screening and triage test for pulmonary TB." PLoS ONE [Electronic Resource] 17(12): e0277393	Intervention (assessment of diagnostic strategies)
Bastos, H. N., et al. (2016). "A Prediction Rule to Stratify Mortality Risk of Patients with Pulmonary Tuberculosis." PLoS ONE [Electronic Resource] 11(9): e0162797	Study design (not an economic evaluation)
Chew, R., et al. (2022). "Modelling the cost-effectiveness of pulse oximetry in primary care management of acute respiratory infection in rural northern Thailand." Tropical Medicine and International Health 27(10): 881-890	Population (includes children)
Chouaid, C., et al. (1995). "Cost-analysis of four diagnostic strategies for Pneumocystis carinii pneumonia in HIV-infected subjects." European Respiratory Journal 8(9): 1554-1558	Intervention (assessment of diagnostic strategies)
Fan, L., et al. (2014). "Semiquantitative cough strength score and associated outcomes in noninvasive positive pressure ventilation patients with acute exacerbation of chronic obstructive pulmonary disease." Respiratory Medicine 108(12): 1801-1807	Intervention (hospital inpatient setting)
Huijskens, E. G. W., et al. (2014). "The value of signs and symptoms in differentiating between bacterial, viral and mixed aetiology in patients with community-acquired pneumonia." Journal of Medical Microbiology 63(Pt 3): 441-452	Intervention (assessment of diagnostic strategies) Study design (not an economic evaluation)
Melhuish, A., et al. (2020). "Cost evaluation of point-of-care testing for community-acquired influenza in adults presenting to the emergency department." Journal of Clinical Virology 129: 104533	Intervention (assessment of diagnostic strategies)
Nsengiyumva, N. P., et al. (2021). "Triage of Persons With Tuberculosis Symptoms Using Artificial Intelligence-Based Chest Radiograph Interpretation: A Cost-Effectiveness Analysis." Open Forum Infectious Diseases 8(12) (no pagination)(ofab567)	Intervention (assessment of diagnostic strategies)

Spaeth, B., et al. (2019). "Impact of point-of-care testing for white blood cell count on triage of patients with infection in the remote Northern Territory of Australia." PATHOLOGY 51(5): 512-517	Intervention (assessment of diagnostic strategies)
van de Maat, J., et al. (2020). "Cost Study of a Cluster Randomized Trial on a Clinical Decision Rule Guiding Antibiotic Treatment in Children With Suspected Lower Respiratory Tract Infections in the Emergency Department." Pediatric Infectious Disease Journal 39(11): 1026-1031	Population (includes children)
Webb, B. J., et al. (2019). "Antibiotic Use and Outcomes After Implementation of the Drug Resistance in Pneumonia Score in ED Patients With Community-Onset Pneumonia." Chest 156(5): 843-851	Study design (not an economic evaluation)