National Institute for Health and Care Excellence

Pneumonia: diagnosis and management (update)

[F] Evidence reviews for non-invasive respiratory support for hospitalised patients with pneumonia

NICE guideline [number]
Evidence reviews underpinning recommendations 1.9.1 to 1.9.3 in the NICE guideline

April 2025

Draft for consultation

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ISBN: xxx

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The clinical and cost effectiveness of different types of non-invasive respiratory support compared to each other or usual care for hospitalised patients with pneumonia

1.1 Review question

In people with community- or hospital-acquired pneumonia managed in hospital, what is the clinical and cost effectiveness of one type of non-invasive respiratory support (for example, non-invasive ventilation, continuous positive airway pressure or high flow nasal oxygen) compared with another type of non-invasive respiratory support intervention or usual care?

1.1.1 Introduction

1.1.2 Summary of the protocol

Table 1.1: PICOS inclusion criteria

Population	Inclusion: Babies over 28 days (corrected gestational age), children, young people (age <18 years) and adults (≥18 years) with pneumonia (community or hospital acquired) requiring management in hospital. Exclusion: • Babies up to and including 28 days (corrected gestational age). • People with COVID-19 pneumonia. • People who acquire pneumonia while intubated (ventilator-associated pneumonia). • People who are severely immune-compromised (have a primary immune deficiency or secondary immune deficiency related to HIV infection, or severe drug or systemic disease-induced immunosuppression, for example, people who have taken immunosuppressant cancer therapy or undergone organ transplantation). • People in whom pneumonia is an expected terminal event. • People with non-pneumonic infective exacerbations of bronchiectasis. • People with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • People with pneumonia associated with cystic fibrosis.

	• People with aspiration pneumonia as a result of inhaling a large bolus of gastric contents.
Interventions	Non-invasive respiratory support: • Continuous positive airway pressure (CPAP) • Non-invasive ventilation (NIV) • High flow oxygen therapy (also called high flow nasal cannulae [HFNC]. This method delivers warmed and humidified oxygen at high flow through nasal cannulae). Exclusion: • The use of non-invasive ventilation for weaning from intubation
Comparator	Usual care – oxygen therapy and all other supportive measures, short of assisted ventilation.
Outcomes	Primary: • Mortality at 30 days from initiation of respiratory support • Need for intubation / invasive ventilation (tracheostomy or oral endotracheal tube) • ICU admission • Length of hospital or ICU stay • Duration of ventilatory assistance • Hospital readmission within 30 days Secondary: • Clinical cure (at end of follow-up) • Complications within 30 days of hospital discharge (composite of empyema, effusion, abscess, metastatic infection, superinfection, multiorgan dysfunction syndrome, pneumothorax). • Health related quality of life (measured by CAP symptom questionnaire, EQ5D, or SF-36) • Adverse events
Study type	RCTs Protocol deviation: Prospective cohort studies

For the full protocol see appendix A.

1.1.3 Methods and process

Protocol deviations

The protocol stated that in any meta-analyses where some (but not all) of the data comes from indirect studies, a sensitivity analysis will be conducted, excluding those studies from the analysis. Although this was the case, the committee did not require this analysis because

the 1 study that was indirectly applicable (due to the population) was the only study that used HFNC, which the committee chose to focus on.

Searches

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

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

The searches for effectiveness evidence were run on 31 January 2024 and topped up on 23 February 2024. An effectiveness search was done covering adults and a separate strategy was run for children and young people.

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

The database searches were supplemented with additional search methods. Reference list checking and forward citation searching were conducted on Web of Science Core Collection on 30 January 2024 using seed references identified from the scoping searches and the search for systematic reviews.

A further search covering cohort studies for adults and children was run on 2 July 2024 in the same databases (CENTRAL, Embase and MEDLINE ALL), applying the same limits as above. Standard NICE filters were used to limit to cohort studies. This was done as a protocol deviation following committee consensus that the RCT evidence was insufficient for them to be confident making recommendations.

The searches for cost effectiveness evidence were run on 20 November 2023 and re-run on 14 October 2024 for papers published since 2014. The following databases were searched: Econlit (Ovid); Embase (Ovid); International HTA Database (https://database.inahta.org); MEDLINE ALL (Ovid); and NHS Economic Evaluation Database (NHS EED) (CRD). The same limits as in the effectiveness search were used. The validated NICE Cost Utility Filter was used on MEDLINE and Embase. Validated NICE filters were used in MEDLINE and Embase to remove references exclusively set in countries that are not OECD members.

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

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

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

Searches were conducted separately for adults and for babies, children and young people (see appendix B for the literature search strategy). The searches found 1,636 records for adults and 1,252 records for babies, children and young people.

These references were screened at title and abstract level against the review protocol, with 1,619 excluded at this level for adults and 1,236 excluded at this level for babies, children and young people. 10% of references were screened separately by two reviewers with 100% agreement.

The full texts of 17 RCTs for adults and 16 RCTs for babies, children and young people were ordered for closer inspection. 3 of these studies met the criteria specified in the review protocol (appendix A) for adults and 2 for babies, children and young people. 2 Studies were included from a previous version of this guideline for adults giving a total of 7 studies, 5 for adults and 2 for children. For a summary of the included studies see Tables 2 and 3.

In consideration of the limited RCT evidence identified a second search was conducted to search for prospective cohort studies, as a protocol deviation. This search found 3001 records combined for adults and babies, children and young people. The references were screened at title and abstract level, and 2946 records were excluded. The full texts of 55 cohort studies were ordered, and one study in adults met the criteria to be included.

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

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

1.1.4.2 Excluded studies

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

1.1.5 Summary of studies included in the effectiveness evidence

Table 2: Summary of studies included for adults

Study details	Population	Intervention	Comparison	Outcomes	Risk of bias
RCT studies from previous guideline					
Confalonieri 1999 Italy	Total N=56 Severe CAP. Acute respiratory failure. In ICU.	**CPAP** Face mask: pressure support ventilation (PSV) 5 to 10 cm H2O. Settings were adjusted on the basis of continuous oximetry. N=28	**Standard oxygen** Venturi mask: adjusted to achieve arterial oxygen saturation above 90%. N=28	• Mortality • Need for invasive ventilation • Duration of hospital stay • Duration of ventilation • Adverse events	Low Directly applicable
Cosentini 2010 Italy	Total N= 47 CAP moderate hypoxemic acute respiratory failure. Admitted to emergency departments.	**CPAP** High-flow generator (90 to 140 L/min) with helmet. PEEP: 10 cm H2O. FiO2 set to maintain pulse oximetry 92%. N=20	**Standard oxygen** Venturi mask: FiO2 to maintain pulse oximetry 92% N=27	• Mortality • Need for invasive ventilation • Adverse events	High Directly applicable
New RCT studies					
Brambilla 2014 Italy	Total N= 81 Severe hypoxemic respiratory failure due to pneumonia. Admitted to high dependency unit	**CPAP** CPAP helmet: initial PEEP of 10 cm H20 and an FiO2 set in order to maintain SpO2 ≥92%. N=40	**Standard oxygen** Venturi mask: FiO2 set to maintain SpO2 ≥92%. N=41	• Mortality • Need for invasive ventilation • Duration of hospital stay • Adverse events	Low Directly applicable

Study details	Population	Intervention	Comparison	Outcomes	Risk of bias
Frat 2015 France and Belgium	Total N=310 Acute Hypoxemic Respiratory Failure (75.6% CAP or HAP). In ICU.	**NIV** face mask connected to an ICU ventilator, with pressure support in non-invasive ventilation mode. PEEP between 2 and 10 cm of water, set to maintain Spo2 of 92% or more. N=110 **High flow nasal oxygen** Large-bore binasal prongs: gas flow rate of 50 litres per minute. FiO2 set to maintain SpO2 >92%. N = 106	**Standard oxygen** Nonrebreather face mask: flow rate of 10 litres per minute or more, set to maintain SpO2 ≥92%. n = 94	• Mortality • Need for invasive ventilation • Adverse events	Low Indirectly applicable
He 2019 China	Total N=200 Pneumonia-induced early mild acute respiratory distress syndrome. In respiratory and critical care departments	**BiPAP** Bilevel positive airway pressure S/T mode, oral-nasal face mask: Expiratory positive airway pressure set at 4 cm H2O and increased by 1–2-cm H2O increments, Inspiratory positive airway	**Standard oxygen** Venturi mask: Oxygen flow and FiO2 set to maintain SpO2 92-96%. N=98	• Mortality • Need for invasive ventilation • Duration of hospital stay • Adverse events	Low Directly applicable

Study details	Population	Intervention	Comparison	Outcomes	Risk of bias
		pressure adjusted to obtain a tidal volume between 6 mL/kg and 10 mL/kg, FiO2 set to maintain SpO2 92-96%. N=102			
New prospective cohort studies					
Brambilla 2019 Italy	Total N= 347 Acute respiratory failure due to pneumonia (85.4% CAP, 14.5% HAP)	**CPAP** Set according to standard operating procedures N=176	**NPPV** Non-invasive positive pressure ventilation set according to standard operating procedures N=171	• Mortality • Need for invasive ventilation	Low Indirectly applicable

Abbreviations:
CPAP: Continuous positive airway pressure
NPPV: Non-invasive positive pressure ventilation
PEEP: Positive end-expiratory pressure
PSV: pressure support ventilation
BiPAP: Bilevel positive airway pressure

Table 3: Summary of studies included for babies, children and young people

Study details	Population	Intervention	Comparison	Outcomes (risk of bias)	Risk of bias
Liu 2020 China	N=84 Pneumonia and mild to moderate respiratory failure Aged under 2	**High flow nasal oxygen** Warm humidification high flow double chamber nasal oxygen therapy ventilator: 50-60% oxygen concentration, flow set at 2 L/kg/min to 20 L/min to maintain oxygen saturation ≥92–94%. N=43	**CPAP** 50–60% oxygen concentration, pressure set at 4–6 cm H2O, flow rate set at 5–10 L/min to maintain oxygen saturation ≥92–94% N=41	• Mortality • Need for invasive ventilation • Duration of hospital stay • Duration of ventilation • Adverse events • ICU admission	Low Indirectly applicable
Maitland 2021 (COAST) Kenya and Uganda	N=1115 severe pneumonia plus hypoxaemia (severe and non-severe) Aged 28 days to 12 years	**High flow nasal oxygen** high flow warmed and humidified air/ oxygen blend: Initiated on FiO2 of 21% with flow rates increase and oxygen titrated. Severe N=194 Non-severe N=363	**Standard oxygen** nasal canulae/prongs and escalated to higher flow rates delivered by standard masks. Severe N=194 Non-severe N=364	• Mortality • Duration of hospital stay • Adverse events • Re-hospitalisation	High Partially applicable

Abbreviations:
CPAP: Continuous positive airway pressure

See Appendix D for full evidence tables.

1.1.6 Summary of the effectiveness evidence

Table 2a: GRADE evidence summary for RCTs of non-invasive ventilation vs standard oxygen in adults

Outcomes	No of Participants (studies)	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Interpretation of effect
				Risk with Standard oxygen	Risk difference with NIV (95% CI)	
Mortality	694 (5 studies[1,2,3,4,5])	⨁⊖⊖⊖ **VERY LOW**[6,7] due to indirectness, imprecision	**RR 0.83** (0.53 to 1.31)	**146 per 1000**	**25 fewer per 1000** (from 69 fewer to 45 more)	Could not differentiate between arms
Mortality - CPAP	184 (3 studies[1,2,3])	⨁⊖⊖⊖ **VERY LOW**[7,8] due to inconsistency, imprecision	**RR 0.66** (0.17 to 2.57)	**135 per 1000**	**46 fewer per 1000** (from 112 fewer to 213 more)	Could not differentiate between arms
Mortality - other NIV	510 (2 studies[4,5])	⨁⊖⊖⊖ **VERY LOW**[6,7,9] due to inconsistency, indirectness, imprecision	**RR 0.86** (0.5 to 1.47)	**151 per 1000**	**21 fewer per 1000** (from 76 fewer to 71 more)	Could not differentiate between arms

Met intubation criteria	337 (3 studies[1,2,4])	**VERY LOW**[10,11] due to inconsistency, imprecision	**RR 0.46** (0.18 to 1.14)	**311 per 1000**	**168 fewer per 1000** (from 255 fewer to 44 more)	Could not differentiate between arms
Intubation carried out	694 (5 studies[1,2,3,4,5])	**VERY LOW**[11,12] due to indirectness, imprecision	**RR 0.88** (0.64 to 1.21)	**229 per 1000**	**28 fewer per 1000** (from 83 fewer to 48 more)	Could not differentiate between arms
Intubation carried out - CPAP	184 (3 studies[1,2,3])	⊕⊖⊖⊖ **VERY LOW**[7,9] due to inconsistency, imprecision	**RR 0.63** (0.17 to 2.36)	**156 per 1000**	**58 fewer per 1000** (from 130 fewer to 212 more)	Could not differentiate between arms
Intubation carried out - other NIV	510 (2 studies[4,5])	⊕⊖⊖⊖ **VERY LOW**[11,12] due to indirectness, imprecision	**RR 0.96** (0.74 to 1.24)	**266 per 1000**	**11 fewer per 1000** (from 69 fewer to 64 more)	Could not differentiate between arms
Duration of hospital stay	256 (2 studies[2,4])	⊕⊕⊕⊕ **HIGH**		The mean duration of hospital stay in the intervention groups was **0.96 lower** (1.94 lower to 0.02 higher)		Could not differentiate between arms
Adverse events	694 (5 studies[1,2,3,4,5])	⊕⊕⊖⊖ **LOW**[7]	**RR 0.73** (0.41 to 1.31)	**80 per 1000**	**22 fewer per 1000**	Could not differentiate between arms

		due to imprecision			(from 47 fewer to 25 more)	
Adverse events - CPAP	184 (3 studies[1,2,3])	⊕⊕⊖⊖ **LOW**[7] due to imprecision	**RR 0.25** (0.03 to 2.1)	**42 per 1000**	**31 fewer per 1000** (from 40 fewer to 46 more)	Could not differentiate between arms
Adverse events - other NIV	510 (2 studies[4,5])	⊕⊕⊖⊖ **LOW**[7] due to imprecision	**RR 0.8** (0.44 to 1.46)	**99 per 1000**	**20 fewer per 1000** (from 55 fewer to 46 more)	Could not differentiate between arms
Duration of intubation	20 (1 study[2])	⊕⊕⊖⊖ **LOW**[13] due to inconsistency		The mean duration of intubation in the intervention groups was **3 lower** (5.87 to 0.13 lower)		Favours NIRS

[1] Brambilla 2014
[2] Confalonieri 1999
[3] Cosentini 2010
[4] He 2019
[5] Frat 2015
[6] Downgraded once as greater than 33.3% of the weight in the meta-analysis came from indirect or partially direct studies (Frat 2015)
[7] Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)
[8] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 58%)
[9] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 34%)
[10] Downgraded twice as the I2 was greater than 66.7% (I2 = 75%)
[11] Downgraded once as 95%CI crosses one clinical decision threshold (0.8)

[12] Downgraded twice as greater than 66.6% of the weight in the meta-analysis came from indirect or partially direct studies (Frat 2015)
[13] Downgraded twice due to small sample size from a single study
Abbreviations:
CPAP: Continuous positive airway pressure
NIV: Non-invasive ventilation

Table 4b: GRADE evidence summary for prospective cohort studies of CPAP vs NPPV in adults

Outcomes	No of Participants (studies)	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Interpretation of effect
				Risk with NPPV	Risk difference with CPAP (95% CI)	
Mortality	347 (1studies[1])	⨁⊖⊖⊖ **VERY LOW**[2,3,4] due to inconsistency, indirectness, imprecision	**RR 1.04** (0.72 to 1.51)	**234 per 1000**	**9 more per 1000** (from 65 fewer to 122 more)	Could not differentiate between arms
Need for invasive ventilation	347 (1studies[1])	⨁⊖⊖⊖ **VERY LOW**[2,3,4] due to inconsistency, indirectness, imprecision	**RR 0.84** (0.47 to 1.49)	**129 per 1000**	**21 fewer per 1000** (from 68 fewer to 63 more)	Could not differentiate between arms

[1] Brambilla 2019
[2] Downgraded once for inconsistency: single study
[3] Downgraded once for indirectness: single study rated as being indirectly applicable due to no control group
[4] Downgraded twice for imprecision: 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)

Table 5: GRADE evidence summary for RCTs of high flow nasal cannula vs CPAP in babies, children and young people

Outcomes	No of Participants (studies)	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Interpretation of effect
				Risk with CPAP	Risk difference with HFNC (95% CI)	
Mortality	84 (1 study[1])	⨁⨁⨀⨀ **LOW**[2,3] due to inconsistency, indirectness	Not estimable	Not estimable	Not estimable	Could not differentiate between arms
Intubation carried out	84 (1 study[1])	⨁⨀⨀⨀ **VERY LOW**[2,3,4] due to inconsistency, indirectness, imprecision	**RR 1.43** (0.43 to 4.7)	**98 per 1000**	**42 more per 1000** (from 56 fewer to 361 more)	Could not differentiate between arms
Duration of hospital stay	84 (1 study[1])	⨁⨀⨀⨀ **VERY LOW**[2,3] due to inconsistency, indirectness, imprecision		The mean duration of hospital stay in the intervention groups was **0 higher** (0.43 lower to 0.43 higher)		Could not differentiate between arms
Adverse events	84 (1 study[1])	⨁⨁⨀⨀ **LOW**[2,3] due to inconsistency, indirectness	**RR 0.17** (0.04 to 0.74)	**268 per 1000**	**223 fewer per 1000** (from 70 fewer to 258 fewer)	Favours HFNC

Duration of intubation	10 (1 study[1])	⨁⨁⊖⊖ **LOW**[2,3] due to inconsistency, indirectness		The mean duration of intubation in the intervention groups was **1 lower** (1.63 to 0.37 lower)		Favours HFNC
ICU admission	84 (1 study[1])	⨁⊖⊖⊖ **VERY LOW**[2,3,4] due to inconsistency, indirectness, imprecision	**RR 1.43** (0.43 to 4.7)	**98 per 1000**	**42 more per 1000** (from 56 fewer to 361 more)	Could not differentiate between arms

[1] Liu 2020
[2] Downgraded once for inconsistency: single study
[3] Downgraded once for indirectness: single study rated as being indirectly applicable due to no control group
[4] Downgraded twice for imprecision because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)

Table 6: GRADE evidence summary for RCTs of high flow nasal cannula vs standard oxygen in babies, children and young people

Outcomes	**No of Participants (studies)** Follow up	**Quality of the evidence** (GRADE)	**Relative effect (95% CI)**	**Anticipated absolute effects**		**Interpretation of effect**
				Risk with Standard oxygen	**Risk difference with HFNC** (95% CI)	
Mortality	1110 (1 study[1])	⨁⊖⊖⊖ **VERY LOW**[2,3,4,5] due to risk of bias, inconsistency, indirectness, imprecision	**RR 0.79** (0.56 to 1.12)	**108 per 1000**	**23 fewer per 1000** (from 48 fewer to 13 more)	Could not differentiate between arms

Duration of hospitalisation	1115 (1 study[1])	⨁⊖⊖⊖ **VERY LOW**[2,3,4] due to risk of bias, inconsistency, indirectness		The mean duration of hospitalisation in the intervention groups was **0.25 higher** (0.56 lower to 1.07 higher)		Could not differentiate between arms
Adverse events	1115 (1 study[1])	⨁⊖⊖⊖ **VERY LOW**[2,3,4,5] due to risk of bias, inconsistency, indirectness, imprecision	**RR 0.92** (0.68 to 1.24)	**133 per 1000**	**11 fewer per 1000** (from 42 fewer to 32 more)	Could not differentiate between arms
Hospital re-admission	1002 (1 study[1])	⨁⊖⊖⊖ **VERY LOW**[2,3,4,6] due to risk of bias, inconsistency, indirectness, imprecision	**RR 1.25** (0.47 to 3.34)	**14 per 1000**	**4 more per 1000** (from 8 fewer to 33 more)	Could not differentiate between arms

[1] Maitland 2021
[2] Downgraded twice for risk of bias: single study at high risk of bias
[3] Downgraded once for inconsistency: single study
[4] Downgraded once for indirectness: single study only partially applicable
[5] Downgraded once as 95%CI crosses one clinical decision threshold (0.8)
[6] Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)

See appendix F for full GRADE tables.

1.1.7 Evidence statements (for evidence that was not suitable for GRADE assessment)

One RCT (Brambilla 2014) of 81 adults, at low risk of bias, found no significant difference in duration of hositalisation between CPAP (median 14.5 days, IQR 10.8–24.3, n = 38) and standard oxygen (median 14 days, IQR 10.0–16.0, n = 34) for adults, p=0.12.

1.1.8 Economic evidence

1.1.8.1 Included studies

A single search was performed to identify published economic evaluations of relevance to any of the questions in this guideline update. See Appendix B – Literature search strategies for the search strategy.

This search retrieved 3,201 studies. Based on title and abstract screening, 3,168 of the studies could confidently be excluded for this question. Thirty-three studies were excluded following the full-text review. Leaving no included studies for this review question. See Appendix G – Economic evidence study selection for the study selection process.

1.1.8.2 Excluded studies

See **Error! Reference source not found.**for a list of excluded studies, with reason for exclusion.

1.1.9 Summary of included economic evidence

There are no included studies in this review question.

1.1.10 Economic model

No original economic modelling was completed for this review question.

1.1.11 Unit costs

No unit costs were supplied for this review question.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1 The outcomes that matter most

The committee noted that reducing the need for mechanical ventilation would be the most impactful benefit of non-invasive respiratory support (NIRS), this would both be a likely benefit to patients and potentially reduce the demand for ICU beds. For this reason they were also interested in admission to ICU and duration of ICU stay. The other key outcome was mortality at 30 days from initiation of respiratory support because of the mortality risk from severe pneumonia.

1.1.12.2 The quality of the evidence

The overall quality of the evidence tended to be poor. GRADE was applied to the findings and determined that in adults 3 findings were of very low quality (for the outcomes of mortality within 30 days; met criteria for intubation; intubation carried out) 1 was of low quality (duration of intubation) and 1 was of high quality (duration of hospital stay). The main reasons for downgrading were imprecision and inconsistency with a number of small studies, with some that were only partially applicable to this review question. When cohort studies were added to expand the evidence review, this did not change the overall quality as only one study was added which provided very low quality evidence on mortality and intubation rates.

In babies, children, and young people, 3 findings for high flow nasal cannula (HFNC) compared to continuous positive airways pressure (CPAP) were of very low quality (for the outcomes of intubation carried out; duration of hospital stay; ICU admission) and 2 were of low confidence (for the outcomes of duration of intubation; adverse events), and all findings for HFNC compared to standard oxygen were of low quality (for the outcomes of mortality within 30 days; duration of hospital stay; hospital readmission; adverse events). The evidence for babies, children, and young people was limited by a lack of studies. The COAST trial was indirectly relevant to this review question as it was conducted in a low resource setting with a population with higher comorbidities (malnutrition, HIV, malaria etc.). The committee also raised concerns that Liu (2020) was conducted in China during the early stages of the COVID-19 pandemic, so it is possible that a portion of their sample had been misdiagnosed.

The committee noted that the limited evidence base and overall low quality of the evidence made it difficult to base any recommendations on it. They also found the lack of significant effects to be contrary to their clinical experience which in addition to the other limitations in the evidence base cast doubt on the robustness of the findings. They discussed that the trials were underpowered, and that further research may be likely to show the benefits of these interventions in people with pneumonia.

The committee further noted caution about the availability of evidence in hospital settings (especially ICU), as many patients are classified under the more general label of respiratory failure and only later formally diagnosed as having pneumonia. This means the evidence available for review is likely to be limited.

1.1.12.3 Benefits and harms

The committee agreed that the idea of non-invasive respiratory support as an umbrella term for these interventions was problematic because interventions like high-flow nasal oxygen are fairly simple interventions that do not require extensive staff training, and are comfortable and easy to use for patients, whereas interventions like CPAP and NIV were quite burdensome to both staff and patients. For this reason they decided it was important to consider them separately. The findings that NIRS did not increase mortality (within 30 days) or adverse events compared to

standard oxygen were reassuring to the committee in that they suggested there is no harm associated with using these interventions. The committee did note that there are concerns raised around the use of NIV and CPAP due to adverse events. The committee discussed that these have been reported in studies of respiratory failure in the wider literature, which could potentially be extrapolated to a pneumonia population. The committee expressed a preference for HFNC as they noted that it is more comfortable and easier to use, allows the person to eat and drink as usual, and has fewer potential safety concerns when compared to CPAP or NIV. They noted that the evidence did not discriminate between these interventions.

The committee were particularly interested in outcomes relating to mechanical intervention. Although there was no significant effect identified in the included studies on the number of patients intubated or the number who met the criteria for intubation, there was a reduction in the duration of mechanical ventilation for those who were intubated in adults and in babies, children, and young people, indicating a possible benefit in this area. In light of the lack of serious harm and the potential benefits the committee reported from their experience, they decided to make a consensus recommendation to consider a trial of HFNC when standard oxygen therapy is not effective before proceeding to intubation. They expressed the view that it was of greater benefit to ensure clinicians have the option to use it even though the evidence is poor than to wait until more evidence is available to strengthen the recommendation. They noted that for patients who had co-existing pathology such as COPD or acute pulmonary oedema, NIV or CPAP might also be options for a trial.

Lay members emphasised the importance of respecting patient preferences. They described the discomfort of CPAP compared to the less invasive experience of HFNC and expressed the need to ensure individuals have information and support to make choices about the balance between their clinical needs with their comfort. The committee agreed that this was an important part of creating escalation plans and considering clinical trajectory. They also discussed the importance of ‘ceilings of care’, in relation to respiratory support for people with a very poor prognosis because of, for example, frailty or co-morbidities. They agreed that because of this, it was important to involve the multidisciplinary team in decisions about offering non-invasive support and to consider the risk of failure and the clinical trajectory to help decide whether a person could be cared for in a ward environment, perhaps with the support of a critical care team, or whether they should be cared for in a high dependency or intensive treatment unit. They discussed that HFNC may be easier to deliver in non-ICU settings than CPAP or NIV but noted that hospitals are likely to have the resources to deliver NIV or CPAP in acute care areas.

The committee highlighted the specific benefits of having further treatment options for patients who are unable or unwilling to be intubated due to the risks associated with sedation, which underlined the decision to recommend considering NIRS as an alternative intervention that could be tried and to take into account the clinical trajectory of the patient.

1.1.12.4 Cost effectiveness and resource use

There was no existing cost effectiveness evidence for this review question. The committee explained that there is a substantial variation in the use of non-invasive respiratory support across the country, and they expressed the view it was important to address this issue.

The committee explained that NIV and CPAP can be costly due to the additional nursing support required. The committee also acknowledged that it can be very unpleasant for people, temporarily lowering their quality of life.

The committee noted that statistical significance was not reached for most outcomes in the effectiveness review, and that there was only a tendency toward improvement for some outcomes. Due to this, and potentially high interventions costs, the committee expressed the view that they lacked sufficient evidence to recommend NIV or CPAP for everyone. Instead, they limited their recommendation to people for whom standard oxygen therapy is not effective. Therefore, given that this recommendation will apply only to a subset of people on a trial basis and where equipment is already available, it will not result in a significant resource impact on the NHS.

The committee referred to their positive collective experience using high flow nasal oxygen support during the COVID-19 pandemic. They noted that, due to its widespread use during the pandemic, hospitals are likely to already have the equipment, resources and experience to implement the recommendation without incurring additional costs for acquiring equipment. It was noted that this recommendation applies only to a subset of more severe patients who may benefit, and it is intended as a trial. The committee were of a view that any additional costs would be offset by potentially improved outcomes, including decreased mortality in people with severe pneumonia.

1.1.12.5 Other factors the committee took into account

The committee noted that current practice often includes the use of HFNC and that recommending this would not constitute a change in practice. Instead, they believed that the recommendation would provide clarification that the current use of HFNC is appropriate.

1.1.13 References – included studies

1.1.13.1 Effectiveness

Confalonieri, M., Potena, A., Carbone, G., Porta, R. D., Tolley, E. A., & Umberto Meduri, G. (1999). Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of non-invasive ventilation. *American journal of respiratory and critical care medicine*, *160*(5 Pt 1), 1585–1591.

Cosentini, R., Brambilla, A. M., Aliberti, S., Bignamini, A., Nava, S., Maffei, A., Martinotti, R., Tarsia, P., Monzani, V., & Pelosi, P. (2010). Helmet continuous positive airway pressure vs oxygen therapy to improve oxygenation in community-acquired pneumonia: a randomized, controlled trial. *Chest*, *138*(1), 114–120.

Brambilla, Anna Maria, Aliberti, Stefano, Prina, Elena et al. (2014) Helmet CPAP vs. oxygen therapy in severe hypoxemic respiratory failure due to pneumonia. Intensive care medicine 40(7): 942-9

Frat, Jean-Pierre, Ricard, Jean-Damien, Quenot, Jean-Pierre et al. (2019) Non-invasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation of patients with acute hypoxaemic respiratory failure: a randomised, multicentre, open-label trial. The Lancet. Respiratory medicine 7(4): 303-312

He, Hangyong, Sun, Bing, Liang, Lirong et al. (2019) A multicenter RCT of non-invasive ventilation in pneumonia-induced early mild acute respiratory distress syndrome. Critical care (London, England) 23(1): 300

Liu, Cong, Cheng, Wei Yu, Li, Jun Shao et al. (2020) High-Flow Nasal Cannula vs. Continuous Positive Airway Pressure Therapy for the Treatment of Children <2 Years With Mild to Moderate Respiratory Failure Due to Pneumonia. Frontiers in pediatrics 8: 590906

Maitland, K Kiguli, S Olupot-Olupot, P Hamaluba, M Thomas, K Alaroker, F Opoka, RO Tagoola, A Bandika, V Mpoya, A Mnjella, H Nabawanuka, E Okiror, W Nakuya, M Aromut, D Engoru, C Oguda, E Williams, TN Fraser, JF Harrison, DA Rowan, K (2021) Randomised controlled trial of oxygen therapy and high-flow nasal therapy in African children with pneumonia. INTENSIVE CARE MEDICINE 47(5): 566 – 576

Brambilla, Anna Maria, Prina, Elena, Ferrari, Giovanni et al. (2019) Non-invasive positive pressure ventilation in pneumonia outside Intensive Care Unit: An Italian multicenter observational study. European journal of internal medicine 59: 21-26

Appendices

Appendix A – Review protocol

Review title	The clinical and cost effectiveness of different types of non-invasive respiratory support (e.g., non-invasive ventilation, continuous positive airway pressure or high flow nasal oxygen) compared to each other or usual care for hospitalised patients with pneumonia.
Review question	In people with community- or hospital-acquired pneumonia managed in hospital, what is the clinical and cost effectiveness of one type of non-invasive respiratory support (for example, non-invasive ventilation, continuous positive airway pressure or high flow nasal oxygen) compared with another type of non-invasive respiratory support intervention or usual care?
Objective	To determine the relative clinical and cost-effectiveness of different forms of non-invasive respiratory support in people with CAP or HAP managed in hospital.
Searches	**Overall approach** The searches will comprise the following elements: • a combined search for cost effectiveness evidence covering all review questions in this guideline. • a combined search for systematic reviews covering all review questions in this guideline. • searches for effectiveness evidence specific to this review question, which will be further divided into a search relating to adults and a search covering children and young people. **Searches for cost effectiveness evidence**

	A combined search will be undertaken to cover the cost effectiveness aspects of all the review questions in a single search. The following databases will be searched for the cost effectiveness evidence: • Econlit via Ovid • Embase via Ovid • International HTA database via INAHTA website • MEDLINE ALL via Ovid The sensitive version of the validated NICE cost utility filter will be applied to the MEDLINE and Embase search strategies (Hubbard et al., 2022 [doi: 10.1186/s12874-022-01796-2]). Searches for cost effectiveness evidence will be limited to 2014-current (the searches for NICE guideline CG191 were completed in March 2014). The MEDLINE and Embase searches will be limited to evidence from Organisation for Economic Co-operation and Development (OECD) member states using the validated NICE filter (Ayiku et al., 2021 [doi: 10.5195/jmla.2021.1224]). **Effectiveness evidence: combined search for systematic reviews** The search for systematic reviews relating to all review questions in this guideline will cover reviews published since the searches for NICE guideline CG191 were completed in March 2014. The sources for this will be: • Cochrane Database of Systematic Reviews (CDSR) via Wiley

	• Epistemonikos via https://www.epistemonikos.org/ This is the standard NICE practice agreed by the Guidelines Methods Group in September 2022 for identifying systematic reviews for routine guideline searches. **Effectiveness evidence: searches specific to this review question** The searches for effectiveness evidence specific to this review question will use the following databases: • Cochrane Central Register of Controlled Trials (CENTRAL) via Wiley • Embase via Ovid • MEDLINE ALL via Ovid The principal search strategy will be developed in MEDLINE and then adapted, as appropriate, for use in the other sources listed, taking into account their size, search functionality and subject coverage. To ensure records potentially relevant to the parameters set out in sections 6-10 below are not missed the following will be checked as required: • The reference lists of any appropriate studies identified from the combined systematic reviews search covering all questions in this guideline. • Later citations of any key trials, reviews or protocols identified in the combined systematic reviews search, scoping searches for this guideline, evidence reviews for previous NICE guidelines or the searches specific to this review question. The guideline committee or other stakeholders could also be asked if they are aware of any other potentially relevant studies that could be considered.

	The searches will be split into a strategy covering adults and a separate strategy covering children and young people. The searches relating to adults will be an update of NICE guideline CG191 and will: • be conducted from the date of the last search in March 2014. • have an appropriate validated study filter for randomised controlled trials. As the evidence relating to children and young people has not previously been reviewed, these searches will: • not apply a date limit. • not include any study filters. **Managing all search results** Database functionality will be used, where available, to exclude from all searches: • Animal studies • Editorials, letters, news items and commentaries • Conference abstracts and posters • Registry entries for ongoing clinical trials or those that contain no results • Theses and dissertations • Papers not published in the English language. With the agreement of the guideline committee, the searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion. The information services team at NICE will quality assure the principal search strategy and peer review the other strategies. Any revisions or additional steps will be agreed by the review team before being implemented.

	The full search strategies for all databases will be published in the final review.
Condition or domain being studied	Community- or hospital-acquired pneumonia
Population	Inclusion: Babies over 28 days (corrected gestational age), children, young people (age <18 years) and adults (≥18 years) with pneumonia (community or hospital acquired) requiring management in hospital. • CAP is defined as pneumonia that is acquired outside hospital • HAP is defined as pneumonia that occurs 48 hours or more after hospital admission and is not incubating at hospital admission, or within 10 days of a previous hospital admission for a different problem. Exclusion: • Babies up to and including 28 days (corrected gestational age). • People with COVID-19 pneumonia. • People who acquire pneumonia while intubated (ventilator-associated pneumonia). • People who are severely immune-compromised (have a primary immune deficiency or secondary immune deficiency related to HIV infection, or severe drug or systemic disease-induced immunosuppression, for example, people who have taken immunosuppressant cancer therapy or undergone organ transplantation). • People in whom pneumonia is an expected terminal event.

	• People with non-pneumonic infective exacerbations of bronchiectasis. • People with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • People with pneumonia associated with cystic fibrosis. • People with aspiration pneumonia as a result of inhaling a large bolus of gastric contents.
Intervention/Exposure/Test	Non-invasive respiratory support: • Continuous positive airway pressure (CPAP) • Non-invasive ventilation (NIV) • High flow oxygen therapy (also called high flow nasal cannulae [HFNC]. This method delivers warmed and humidified oxygen at high flow through nasal cannulae). Note: the use of non-invasive ventilation for weaning from intubation is excluded
Comparator/Reference standard/Confounding factors	• Usual care – oxygen therapy and all other supportive measures, short of assisted ventilation. Note: comparisons of different doses or durations of oxygen will not be included.
Types of study to be included	Systematic reviews of RCTs and RCTs Protocol deviation: Prospective cohort studies
Other exclusion criteria	Studies including patients for whom pneumonia was not the most likely aetiology of acute hypoxemic respiratory failure, such as acute COPD or asthma exacerbations, post-lung resection or presence of ventilator associated pneumonia, will be excluded.

Context	The NICE guideline on pneumonia in adults was withdrawn (May 2020) during the COVID-19 pandemic. At that time, COVID-19 pneumonia was the prevalent form of pneumonia in the UK and there were concerns that CG191 was diverting healthcare professionals away from NICE's COVID-19 rapid guideline on pneumonia in adults in the community (now replaced by COVID-19 rapid guideline: managing COVID-19). There was also potential for confusion among guideline users by having 2 NICE guidelines on pneumonia in adults that covered similar topic areas but had different recommendations (NG138 pneumonia (community-acquired): antimicrobial prescribing; and NG139 pneumonia (hospital-acquired): antimicrobial prescribing). Additionally, some recommendations in NICE guideline CG191 were not suitable in the context of the pandemic. The pandemic situation has evolved, and the guideline now needs to be reinstated. However, an update to the guideline is also needed to reflect changes in pneumonia management brought about by COVID-19, and to address the potential impact of this update on 3 other related NICE guidelines, to ensure NICE has cohesive guidelines on COVID and non-COVID pneumonia. The proposed update will focus on amending recommendations in light of the COVID-19 pandemic, and ensuring this guideline aligns with other NICE guidance on COVID and non-COVID pneumonia.
Primary outcomes (critical outcomes)	• Mortality at 30 days from initiation of respiratory support • Need for intubation / invasive ventilation (tracheostomy or oral endotracheal tube) • ICU admission • Length of hospital or ICU stay • Duration of ventilatory assistance • Hospital readmission within 30 days

Secondary outcomes (important outcomes)	• Clinical cure (at end of follow-up) • Complications within 30 days of hospital discharge (composite of empyema, effusion, abscess, metastatic infection, superinfection, multiple organ dysfunction syndrome, pneumothorax). • Health related quality of life (measured by CAP symptom questionnaire, EQ5D, or SF-36) • Adverse events
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. Any disagreements will be resolved by discussion with other members of the technical review team. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow. The priority screening functionality within the EPPI-reviewer software will not be used for this review.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For SRs, the ROBIS (Risk of Bias in Systematic Reviews) checklist will be used. For RCTs, the Cochrane risk of bias (RoB) 2 tool will be used.
Strategy for data synthesis	Where possible, meta-analyses of outcome data will be conducted for all comparators that are reported by more than

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

	analysis will be conducted, excluding those studies from the analysis. GRADE will be used to assess the quality of the outcomes. All outcomes in this review will come from RCTs and will be rated as high quality initially and downgraded from this point. Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically (visually) assess the potential for publication bias. Default MIDs will be used: 0.80 and 1.25 for dichotomous outcomes; 0.5 times the control group SD for continuous outcomes.
Analysis of sub-groups	Analysis of subgroups will be conducted for people with and without underlying lung disease (e.g. COPD or cystic fibrosis in children), where data is available. The following groups will be considered separately if data are available: • CAP and HAP • Age: 0-1; 1-5; 5-18; Adults
Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)

1

Appendix B – Literature search strategies

Background and development

Overall approach

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

- Part 1: Systematic review searches

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

- Part 2: Effectiveness evidence searches

This search was developed separately and tailored to each evidence review. For this review, it was further divided, as in the table 'Overview of the search approach'.

After completion of the main searches for Parts 2A and 2B on 31/1/24, at the meeting GCOMM2 on 13/2/24, the committee requested high-flow oxygen therapy was added to the protocol and a top-up search was run for this on 23/2/24. After further discussion at GCOMM6 on 20/6/24 the committee requested a further search for cohort studies and, as there was overlap with the previous searches, these results were screened in a new EPPI-Review as Part 2C.

Overview of the search approach

Part	Search	Intervention	Population	Date run	Date limits	Study filters applied
Part 1 search (main and re-run)	Systematic reviews	All pneumonia topics	Adults, children and young people	Main: 20/11/23 Re-run: 15/10/24	2014-current	Systematic reviews
Part 2A main search	Effectiveness	NIV	Adults	31/1/24	2014-current	RCTs
Part 2A top up search	Effectiveness	High flow oxygen	Adults	23/2/24	None	None
Part 2B main search	Effectiveness	NIV	Children and young people	31/1/24	None	None
Part 2B top up search	Effectiveness	High flow oxygen	Children and young people	23/2/24	None	None
Part 2C search	Effectiveness	NIV or High flow oxygen	Adults, children	2/7/24	None	Cohort studies

Part	Search	Intervention	Population	Date run	Date limits	Study filters applied
			and young people			
Part 3 search (main and re-run)	Cost effectiveness	All pneumonia topics	Adults, children and young people	Main: 20/11/23 Re-run: 16/10/24	2014-current	Cost utility studies

- Part 3: Cost effectiveness searches

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

Search design and peer review

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

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

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

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

Review management

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

Search limits, restrictions and filters

Formats

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

- Animal studies
- Case reports

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

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

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

OECD countries

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

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

Date limits

A date limit of 2014-current was applied to the Systematic Review (Part 1) and Cost Effectiveness (Part 3) searches. This date limit was used because the searches for NICE CG191 Pneumonia in adults: diagnosis and management (published in December 2014) were last run on 17 March 2014.

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

- Part 2A main search: 1 March 2014 onwards as this was an update of CG191.
- Part 2B top-up search: no date limit as this intervention had not been considered previously.
- Part 2B main search and top-up search: no date limit as this population had not been considered previously.
- Part 2C cohort studies: no date limit as this study type had not been considered previously.

Study-type filters

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

The searches for the Part 2A main search used an RCT filter, as CG191 had included two RCTs. The standard filters in use at NICE were applied. The MEDLINE RCT filter was McMaster Therapy – Medline - "best balance of sensitivity and specificity" version. The standard NICE modifications were used: the MeSH heading randomized controlled trial/ (equivalent to randomized controlled trial.pt) was exploded to capture newer, narrower terms; and the free-text term randomized.mp was changed to randomi?ed.mp. to capture both UK and US spellings.

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

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

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

The searches for Part 2B had no study-type filters, as this population had not been considered previously and it was not clear whether evidence from RCTs would be sufficient.

The searches for Part 2C applied standard NICE filters for cohort studies.

Cost effectiveness searches

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

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

Key decisions

Part 1: Systematic review searches

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

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

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

Parts 1-3: Pneumonia terms

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

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

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

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

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

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

The previous strategies could not be used directly because of changes to Medical Subject Headings (MeSH) since 2019. Using the previous searches would now retrieve all MEDLINE results about COVID-19, as well as pneumonia. We now, therefore, have to choose individual MeSH headings from the hierarchy. The choice of headings was made in conjunction with the technical team in the scoping searches in October 2023. Headings for Aspiration, Lipid, Enzootic and Swine Pneumonia, as well as Pneumocystis and COVID-19 were not included. This approach reduced the number of results with just the population terms from 340,000 with the CG191 approach to 124,000. None of the test set were lost by adopting this approach.

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

At the committee meeting GCOMM1 on 20 December 2023 feedback was received from the committee that rickettsial and cryptogenic organizing pneumonia were not relevant to the UK context and could safely be removed from the search strategies. These terms feature in the

Part 1 systematic review and Part 3 cost effectiveness searches as these were completed before the meeting (and were retained in the re-runs for consistency).

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

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

Part 2: Effectiveness evidence searches

The search results for Parts 2A and 2B were screened in two separate EPPI-Reviewer files. The terms for pneumonia and the interventions were identical in both searches. The date limits and study filters were adjusted for each search as above. The search results for Part 2C (cohorts) were screened in a third EPPI-Reviewer file.

As the searches for Part 2A do not have any age-related terms, there is some overlap with the search results for Part 2B. This was not problematic as the results were being screened separately. The search terms for children and young people in Part 2B were taken directly from a previous search for this guideline (Corticosteroids for treating pneumonia in children search Part 2C).

The test papers were those used in forward citation searching and reference list checking, which were derived from the papers included in this question for CG191, the systematic review search in Part 1 and the papers included in the recent reviews for part 1. The intervention terms found all 10 test papers in MEDLINE for Part 2A and all nine for Part 2B.

The terms for non-invasive ventilation were derived from the search terms used in CG191 and updated for this review (e.g. the term "Helmet ventilation" was added to Emtree in 2020). The terms aimed to cover the interventions listed in the protocol for CG191: non-invasive positive pressure ventilation (NPPV or NIPPV); invasive positive pressure ventilation; BiLevel Positive Airway Pressure (BIPAP); non-invasive positive pressure ventilation (NPPV); variable positive airway pressure (VPAP); and AutoPAP and AutoCPAP (APAP, ACPAP).

The search was structured to find NIV in comparison to usual care but not for usual care in its own right. This meant the search terms were not broadened to cover oxygen inhalation therapy, mechanical ventilation or artificial respiration. This is also why the Emtree term "non-invasive ventilation" was not exploded.

The top-up search for Part 2B aimed to cover all forms of high-flow oxygen therapy.

For Part 2C, the cohort studies filter followed standard NICE practice e.g. they have been used in Tobacco NG209 (Review J: NRT in pregnancy) in March 2019 and Gambling-related harms (NG248) (Review A: Factors) in November 2022. They were originally based on the BMJ MEDLINE cohort study strategy from the BMJ Best Practice Evidence-based medicine (EBM) toolkit and from reviewing the terms used by Waffenschmidt et al.

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

It is unusual to add study filters to CENTRAL strategies, as this source is already pre-filtered, and it is considered a database of RCTs and quasi-RCTs. Testing showed that nearly 211,000 records were indexed with the MeSH Cohort Studies and that translating the MEDLINE filter would retrieve over 466,000. It was felt applying this filter was preferable to removing CENTRAL from the list of sources.

Part 1: Systematic review searches

Database results

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

Re-run results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Database of Systematic Reviews (CDSR)	15/10/2024	Wiley	Cochrane Database of Systematic Reviews Issue 10 of 12, October 2024	8
Epistemonikos	15/10/2024	Epistemonikos	Version available on 15/10/2024	2571

Search strategy history

Database name: Cochrane Database of Systematic Reviews (CDSR)

Searches	
#1	[mh ^pneumonia] or [mh ^bronchopneumonia] or [mh ^pleuropneumonia] or [mh ^"pneumonia, bacterial"] or [mh ^"chlamydial pneumonia"] or [mh ^"pneumonia, mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, rickettsial"] or [mh ^"pneumonia, staphylococcal"] or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"cryptogenic organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"]
	5252

Searches
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15137
#3 #1 or #2 16754
#4 #1 or #2 in Cochrane Reviews 244
#5 #1 or #2 with Cochrane Library publication date Between Jan 2014 and Nov 2023, in Cochrane Reviews 177
Note: in the re-run Line #5 was changed to #1 or #2 with Cochrane Library publication date Between Nov 2023 and Oct 2024, in Cochrane Reviews.

Database name: Epistemonikos

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

Searches

OR non-hospitalised OR "non hospitalized" OR non-hospitalized OR "non hospitalisation" OR non-hospitalisation OR "non hospitalization" OR non-hospitalization))

14 abstract:((pneumonia OR pneumonias) AND (bacterial* OR chlamydial* OR mycoplasma* OR pneumococcal* OR rickettsial* OR staphylococcal* OR staphylococcus* OR necrotiz* OR necrotis* OR viral* OR organizing* OR organising* OR cryptogenic* OR bilateral* OR granulomatous* OR infectious* OR interstitial* OR neonatal* OR obstructive* OR lobar* OR escherichia* OR haemophilus* OR hemophilus* OR influenzae* OR nocardiosis* OR streptococcus* OR streptococcal*))

This is the final search as formatted by Epistemonikos:

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

Results:

Total: 48055

Apply Publication Year limits of 2014-2024: 30820

Download 1: Apply Publication type - Systematic Review: 2307

Searches
Download 2: Apply Publication type - Broad Synthesis: 223 Download 3: Apply Publication type - Structured Summary: 41 **Note:** The re-run search covered the whole timespan 2014-2024 as the phrases in the free text were updated to use a version with a hyphen and to spell out the words rather than truncating them. The main search had used Publication Year limits of 2014-2023.

Part 2A: Effectiveness evidence searches (adults) – main search

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	31/1/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 1 of 12, January 20	269
Embase	31/1/2024	Ovid	Embase 1974 to 2024 January 30	514
MEDLINE ALL	31/1/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to January 30, 2024	235

Additional search techniques

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	30/1/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-28	9
Reference list checking	30/1/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-28	7

Search strategy history

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

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

Searches
or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 5271
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15365
#3 #1 or #2 16986
#4 [mh "positive-pressure respiration"] 3552
#5 [mh ^"non-invasive ventilation"] 644
#6 ((non-invasive* or (non NEXT invasive*) or (positive NEXT pressure*) or (pressure NEXT release*) or helmet*) NEAR/3 (respir* or breath* or ventilat* or airway*)):ti,ab 5797
#7 (((positive NEXT airway*) or (continuous NEXT distend*) or ("positive end" NEXT expiratory*)) NEAR/1 pressur*):ti,ab 6890
#8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP):ti,ab 10447
#9 {or #4-#8} 15521
#10 #3 and #9 972
#11 ((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an 496405
#12 #10 not #11 494
#13 "conference":pt 233734
#14 #12 not #13 386
#15 #12 not #13 in Trials 363
Post search filter: Date added to CENTRAL trials database: 01/03/2014 to 01/02/2024 269

Database name: Embase

Searches
1 pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ or hospital acquired pneumonia/ 319051
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 236505
3 1 or 2 402069
4 positive pressure ventilation/ or exp continuous positive airway pressure/ or exp intermittent positive pressure ventilation/ or exp non-invasive positive pressure ventilation/ or exp positive end expiratory pressure ventilation/ or exp helmet ventilation/ 23433
5 non-invasive ventilation/ 20233
6 ((non-invasive* or "non invasive*" or "positive pressure*" or "pressure release*" or helmet*) adj3 (respir* or breath* or ventilat* or airway*)).ti,ab. 32612

Searches
7 (("positive airway*" or "continuous distend*" or "positive end expiratory*") adj1 pressur*).ti,ab. 30486
8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP).ti,ab. 50910
9 or/4-8 98597
10 3 and 9 9672
11 limit 10 to english language 9184
12 (letter or editorial).pt. 2101460
13 11 not 12 8713
14 Case report/ 2965267
15 13 not 14 6232
16 nonhuman/ not human/ 5375756
17 15 not 16 6013
18 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5822847
19 17 not 18 3925
20 random:.tw. 2028019
21 placebo:.mp. 532702
22 double-blind:.tw. 248967
23 or/20-22 2309138
24 19 and 23 678
25 limit 24 to dc=20140301-20240131 514

Database name: MEDLINE ALL

Searches
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or healthcare-associated pneumonia/ 124672
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 161188
3 1 or 2 231105
4 exp positive-pressure respiration/ 29502
5 non-invasive ventilation/ 3796
6 ((non-invasive* or "non invasive*" or "positive pressure*" or "pressure release*" or helmet*) adj3 (respir* or breath* or ventilat* or airway*)).ti,ab. 19988
7 (("positive airway*" or "continuous distend*" or "positive end expiratory*") adj1 pressur*).ti,ab. 21057
8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP).ti,ab. 27736
9 or/4-8 58701
10 3 and 9 3185
11 limit 10 to english language 2819
12 limit 11 to (letter or historical article or comment or editorial or news or case reports) 607

Searches			
13	11 not 12	2212	
14	Animals/ not (Animals/ and Humans/)		5158442
15	13 not 14	2115	
16	exp Randomized Controlled Trial/		609549
17	randomi?ed.mp.	1102689	
18	placebo.mp.	253380	
19	or/16-18	1169780	
20	15 and 19	346	
21	limit 20 to ed=20140301-20240131		193
22	limit 20 to dt=20140301-20240131		225
23	21 or 22	235	

Additional search techniques

Forward citation searching

Date of search	30/01/2024
How the seed papers were identified	Collated the results from • 2 papers included in CG191 for this question • Systematic reviews identified in Part 1 • The papers included in recent reviews from Part 1
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2015-present)
Date of last update	Data updated 2024-01-28
How results were managed	Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.
How the results were selected	Included potentially relevant papers on NIV for treating pneumonia. Did not make any decisions based on the location of the study. Did not include any papers about COVID-19. Did not include any papers that were: about methods or epidemiology; systematic reviews, animal studies, letters or editorials; not written in English.

	Added to a Marked List and then removed anything that was published before 2014.
List of seed papers used	Brambilla AM et al. (2014) Helmet CPAP vs. oxygen therapy in severe hypoxemic respiratory failure due to pneumonia. Intensive Care Medicine, 40(7), 942-9. Confalonieri M et al. (1999) Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of non-invasive ventilation. American Journal of Respiratory and Critical Care Medicine, 160(5 Pt1), 1585-1591. Cosentini R et al. (2010) Helmet continuous positive airway pressure vs oxygen therapy to improve oxygenation in community-acquired pneumonia: a randomized, controlled trial. Chest, 138(1), 114-120. Ferrer M et al. (2003) Non-invasive ventilation in severe hypoxemic respiratory failure: a randomized clinical trial. American Journal of Respiratory & Critical Care Medicine, 168(12), 1438-44. Klefti G; Hill AT (2020) The benefits of non-invasive ventilation for Community-Acquired Pneumonia: A meta-analysis. QJM: monthly journal of the Association of Physicians, Online ahead of print. Lewis SR et al. (2021) High-flow nasal cannulae for respiratory support in adult intensive care patients Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD010172. Ruzsics I et al. (2022) Non-invasive ventilation improves the outcome in patients with pneumonia-associated respiratory failure: Systematic review and meta-analysis. Journal of Infection and Public Health, 15, 3, 349-359. Vanoni NM et al. (2019) Management of acute respiratory failure due to community-acquired pneumonia: a systematic review. Medical Sciences, 7(1). Wilkes, C; Subhi, R; Graham, HR et al. (2022) Continuous Positive Airway Pressure

	(CPAP) for severe pneumonia in low- and middle-income countries: A systematic review of contextual factors. Journal of Global Health, 12, 10012. Zhang Y et al. (2012) Oxygen therapy for pneumonia in adults. Cochrane Database of Systematic Reviews, (3), CD006607.
No. of results	9

Reference list checking

Date of search	30/01/2024
How the seed papers were identified	Collated the results from • 2 papers included in CG191 for this question • Systematic reviews identified in Part 1 • The papers included in recent reviews from Part 1
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2015-present)
Date of last update	Data updated 2024-01-28
How results were managed	Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.
How the results were selected	Included potentially relevant papers on NIV for treating pneumonia. Did not make any decisions based on the location of the study. Did not include any papers about COVID-19. Did not include any papers that were: about methods or epidemiology; systematic reviews, animal studies, letters or editorials; not written in English. Added to a Marked List and then removed anything that was published before 2014.
List of seed papers used	Brambilla AM et al. (2014) Helmet CPAP vs. oxygen therapy in severe hypoxemic respiratory failure due to pneumonia. Intensive Care Medicine, 40(7), 942-9.

	Klefti G; Hill AT (2020) The benefits of non-invasive ventilation for Community-Acquired Pneumonia: A meta-analysis. QJM: monthly journal of the Association of Physicians, Online ahead of print. Lewis SR et al. (2021) High-flow nasal cannulae for respiratory support in adult intensive care patients Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD010172. Ruzsics I et al. (2022) Non-invasive ventilation improves the outcome in patients with pneumonia-associated respiratory failure: Systematic review and meta-analysis. Journal of Infection and Public Health, 15, 3, 349-359. Vanoni NM et al. (2019) Management of acute respiratory failure due to community-acquired pneumonia: a systematic review. Medical Sciences, 7(1). Wilkes, C; Subhi, R; Graham, HR et al. (2022) Continuous Positive Airway Pressure (CPAP) for severe pneumonia in low- and middle-income countries: A systematic review of contextual factors. Journal of Global Health, 12, 10012.
No. of results	7

Part 2A: Effectiveness evidence searches (adults) – top-up search

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	23/2/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 2 of 12, February 2024	102
Embase	23/2/2024	Ovid	Embase 1974 to 2024 February 22	1018
MEDLINE ALL	23/2/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to February 22, 2024	523

Search strategy history

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

Searches
#1 [mh ^pneumonia] or [mh ^bronchopneumonia] or [mh ^pleuropneumonia] or [mh ^"pneumonia, bacterial"] or [mh ^"chlamydial pneumonia"] or [mh ^"pneumonia, mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, staphylococcal"] or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 4393
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15537
#3 #1 or #2 16778
#4 (High* NEAR/1 (flow* or frequency*) NEAR/4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)):ti,ab 2846
#5 ((highflow* or higherflow* or HF) NEAR/4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)):ti,ab 2263
#6 (HFNC or HFNCT or HHHFNC or HFFM or HFNP):ti,ab 903
#7 {or #4-#6} 3753
#8 #3 and #7 350
#9 ((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an 494409
#10 #8 not #9 149
#11 "conference":pt 236547
#12 #10 not #11 108
#13 #10 not #11 in Trials 102

Database name: Embase

Searches
1 pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ or hospital acquired pneumonia/ 319791
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 237264
3 1 or 2 403008
4 high flow nasal cannula therapy/ 6186
5 humidified high flow nasal cannula therapy/ 186
6 (High* adj1 (flow* or frequency*) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 10663
7 ((highflow* or higherflow* or HF) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 5948

Searches
8 (HFNC or HFNCT or HHHFNC or HFFM or HFNP).ti,ab. 2565
9 or/4-8 19732
10 3 and 9 2878
11 limit 10 to english language 2835
12 (letter or editorial).pt. 2104366
13 11 not 12 2707
14 Case report/ 2969074
15 13 not 14 1638
16 nonhuman/ not human/ 5386407
17 15 not 16 1625
18 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5844635
19 17 not 18 1018

Database name: MEDLINE ALL

Searches
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or healthcare-associated pneumonia/ 124812
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 161695
3 1 or 2 231640
4 (High* adj1 (flow* or frequency*) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 6176
5 ((highflow* or higherflow* or HF) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 3026
6 (HFNC or HFNCT or HHHFNC or HFFM or HFNP).ti,ab. 1379
7 or/4-6 9195
8 3 and 7 743
9 limit 8 to english language 704
10 limit 9 to (letter or historical article or comment or editorial or news or case reports) 180
11 9 not 10 524
12 Animals/ not (Animals/ and Humans/) 5164074
13 11 not 12 523

Part 2B: Effectiveness evidence searches (children and young people) – main search

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register	31/1/2024	Wiley	Cochrane Central Register	81

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
of Controlled Trials (CENTRAL)			of Controlled Trials Issue 1 of 12, January 20	
Embase	31/1/2024	Ovid	Embase 1974 to 2024 January 30	925
MEDLINE ALL	31/1/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to January 30, 2024	503

Additional search techniques

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	30/1/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-28	29
Reference list checking	30/1/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-28	30

Search strategy history

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

Searches
#1 [mh ^pneumonia] or [mh ^bronchopneumonia] or [mh ^pleuropneumonia] or [mh ^"pneumonia, bacterial"] or [mh ^"chlamydial pneumonia"] or [mh ^"pneumonia, mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, staphylococcal"] or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 5271
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15365
#3 #1 or #2 16986
#4 [mh "positive-pressure respiration"] 3552
#5 [mh ^"non-invasive ventilation"] 644
#6 ((non-invasive* or (non NEXT invasive*) or (positive NEXT pressure*) or (pressure NEXT release*) or helmet*) NEAR/3 (respir* or breath* or ventilat* or airway*)):ti,ab 5797
#7 (((positive NEXT airway*) or (continuous NEXT distend*) or ("positive end" NEXT expiratory*)) NEAR/1 pressur*):ti,ab 6890
#8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP):ti,ab 10447

Searches
#9 {or #4-#8} 15521
#10 #3 and #9 972
#11 [mh ^Infant] or [mh ^"Infant Health"] or [mh ^"Infant Welfare"] or [mh ^"Infant Care"] 29408
#12 (infan* or baby* or babies or toddler* or (pre NEXT school*) or preschool* or kindergar*):ti,ab 61124
#13 [mh Child] or [mh "Child Behavior"] or [mh ^"Child Health"] or [mh ^"Child Welfare"] or [mh ^"Child Care"] 79981
#14 [mh ^Minors] 11
#15 (child* or minor or minors or boy* or girl* or kid or kids):ti,ab 184406
#16 [mh "pediatrics"] 1180
#17 (pediatric* or paediatric*):ti,ab 41210
#18 [mh ^Adolescent] or [mh ^"Adolescent Behavior"] or [mh ^"Adolescent Health"] or [mh ^Puberty] 126411
#19 ((under NEXT 18*) or (under NEXT eighteen*)):ti,ab 16834
#20 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or (school NEXT age*) or schoolage* or underage* or (under NEXT age*)):ti,ab 50662
#21 (young* NEAR/1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)):ti,ab 29057
#22 {or #11-#21} 381215
#23 #10 and #22 237
#24 ((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an 496405
#25 #23 not #24 110
#26 "conference":pt 233734
#27 #25 not #26 89
#28 #25 not #26 in Trials 81

Database name: Embase

Searches
1 pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ or hospital acquired pneumonia/ 319051
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 236505
3 1 or 2 402069
4 positive pressure ventilation/ or exp continuous positive airway pressure/ or exp intermittent positive pressure ventilation/ or exp non-invasive positive pressure ventilation/ or exp positive end expiratory pressure ventilation/ or exp helmet ventilation/ 23433

Searches
5 non-invasive ventilation/ 20233
6 ((non-invasive* or "non invasive*" or "positive pressure*" or "pressure release*" or helmet*) adj3 (respir* or breath* or ventilat* or airway*)).ti,ab. 32612
7 (("positive airway*" or "continuous distend*" or "positive end expiratory*") adj1 pressur*).ti,ab. 30486
8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP).ti,ab. 50910
9 or/4-8 98597
10 3 and 9 9672
11 Juvenile/ or exp child/ or child health/ or infant welfare/ or Child Behavior/ or Child Welfare/ or exp child care/ or "minor (person)"/ 3240765
12 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 736069
13 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2653248
14 exp pediatrics/ 129367
15 (pediatric* or paediatric*).ti,ab. 727596
16 exp adolescent/ or adolescent behavior/ or adolescent health/ or exp Puberty/ 1849299
17 elementary student/ or high school student/ or middle school student/ 13327
18 ("under 18*" or "under eighteen*").ti,ab. 7757
19 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or "school age*" or schoolage* or underage* or "under age*").ti,ab. 782167
20 (young* adj1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)).ti,ab. 475154
21 or/11-20 5607563
22 10 and 21 2228
23 limit 22 to english language 2102
24 (letter or editorial).pt. 2101460
25 23 not 24 2047
26 Case report/ 2965267
27 25 not 26 1370
28 nonhuman/ not human/ 5375756
29 27 not 28 1339
30 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5822847
31 29 not 30 925

Database name: MEDLINE ALL

Searches
Searches Results
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or healthcare-associated pneumonia/ 124672

Searches
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 161188
3 1 or 2 231105
4 exp positive-pressure respiration/ 29502
5 non-invasive ventilation/ 3796
6 ((non-invasive* or "non invasive*" or "positive pressure*" or "pressure release*" or helmet*) adj3 (respir* or breath* or ventilat* or airway*)).ti,ab. 19988
7 (("positive airway*" or "continuous distend*" or "positive end expiratory*") adj1 pressur*).ti,ab. 21057
8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP).ti,ab. 27736
9 or/4-8 58701
10 3 and 9 3185
11 Infant/ or Infant Health/ or Infant Welfare/ or Infant Care/ 882042
12 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 618238
13 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ or Child Care/ 2194587
14 Minors/ 2840
15 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2076423
16 exp pediatrics/ 63231
17 (pediatric* or paediatric*).ti,ab. 461264
18 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ or Puberty/ 2239008
19 ("under 18*" or "under eighteen*").ti,ab. 4405
20 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or "school age*" or schoolage* or underage* or "under age*").ti,ab. 610395
21 (young* adj1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)).ti,ab. 347134
22 or/11-21 5010942
23 10 and 22 740
24 limit 23 to english language 635
25 limit 24 to (letter or historical article or comment or editorial or news or case reports) 130
26 24 not 25 505
27 Animals/ not (Animals/ and Humans/) 5158442
28 26 not 27 503

Additional search techniques

Forward citation searching

Date of search	30/01/2024
How the seed papers were identified	Collated the results from • 2 papers included in CG191 for this question

	• Systematic reviews identified in Part 1 • The papers included in recent reviews from Part 1
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2015-present)
Date of last update	Data updated 2024-01-28
How results were managed	Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.
How the results were selected	Included potentially relevant papers on NIV for treating pneumonia. Did not make any decisions based on the location of the study. Did not include any papers about COVID-19. Did not include any papers that were: about methods or epidemiology; systematic reviews, animal studies, letters or editorials; not written in English. Added to a Marked List and then removed anything that was published before 2014.
List of seed papers used	Chisti MJ et al. (2015) Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. Lancet, 386: 1057–1065. Liu C et al. (2020) High-flow nasal cannula vs. continuous positive airway pressure therapy for the treatment of children <2 years with mild to moderate respiratory failure due to pneumonia. Frontiers in Pediatrics, 8 :590906. Mayfield S et al. (2014) High-flow nasal cannula therapy for respiratory support in children Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD009850. McCollum ED et al. (2019) Bubble continuous positive airway pressure for children with high-risk conditions and severe pneumonia in Malawi: an open label,

	randomised, controlled trial. Lancet Respiratory Medicine, 7: 964–74. Rojas-Reyes MX (2014) Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. Cochrane Database of Systematic Reviews, (12), CD005975. Wang ZL et al. (2020) Continuous positive airway pressure in children with severe pneumonia: a meta-analysis. World Journal of Pediatrics, 16, 6, 637-641. Wilson PT et al. (2013) A randomized clinical trial evaluating nasal continuous positive airway pressure for acute respiratory distress in a developing country. Journal of Pediatrics, 162: 988–992. Wilson PT et al. (2017) Continuous positive airway pressure for children with undifferentiated respiratory distress in Ghana: an open-label, cluster, crossover trial. Lancet Global Health, 5: e615–e623. Zhao X et al. (2021) Outcomes of High-Flow Nasal Cannula Vs. Nasal Continuous Positive Airway Pressure in Young Children With Respiratory Distress: A Systematic Review and Meta-Analysis. Frontiers in Pediatrics, 9, 759297.
No. of results	29

Reference list checking

Date of search	30/01/2024
How the seed papers were identified	Collated the results from • 2 papers included in CG191 for this question • Systematic reviews identified in Part 1 • The papers included in recent reviews from Part 1
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present)

	• Emerging Sources Citation Index (2015-present)
Date of last update	Data updated 2024-01-28
How results were managed	Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.
How the results were selected	Included potentially relevant papers on NIV for treating pneumonia. Did not make any decisions based on the location of the study. Did not include any papers about COVID-19. Did not include any papers that were: about methods or epidemiology; systematic reviews, animal studies, letters or editorials; not written in English. Added to a Marked List and then removed anything that was published before 2014.
List of seed papers used	Chisti MJ et al. (2015) Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. Lancet, 386: 1057–1065. Liu C et al. (2020) High-flow nasal cannula vs. continuous positive airway pressure therapy for the treatment of children <2 years with mild to moderate respiratory failure due to pneumonia. Frontiers in Pediatrics, 8 :590906. Mayfield S et al. (2014) High-flow nasal cannula therapy for respiratory support in children Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD009850. McCollum ED et al. (2019) Bubble continuous positive airway pressure for children with high-risk conditions and severe pneumonia in Malawi: an open label, randomised, controlled trial. Lancet Respiratory Medicine, 7: 964–74. Rojas-Reyes MX (2014) Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. Cochrane Database of Systematic Reviews, (12), CD005975. Wang ZL et al. (2020) Continuous positive airway pressure in children with severe

	pneumonia: a meta-analysis. World Journal of Pediatrics, 16, 6, 637-641. Wilson PT et al. (2013) A randomized clinical trial evaluating nasal continuous positive airway pressure for acute respiratory distress in a developing country. Journal of Pediatrics, 162: 988–992. Wilson PT et al. (2017) Continuous positive airway pressure for children with undifferentiated respiratory distress in Ghana: an open-label, cluster, crossover trial. Lancet Global Health, 5: e615–e623. Zhao X et al. (2021) Outcomes of High-Flow Nasal Cannula Vs. Nasal Continuous Positive Airway Pressure in Young Children With Respiratory Distress: A Systematic Review and Meta-Analysis. Frontiers in Pediatrics, 9, 759297.
No. of results	30

Part 2B: Effectiveness evidence searches (adults) – top-up search

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	23/2/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 2 of 12, February 2024	22
Embase	23/2/2024	Ovid	Embase 1974 to 2024 February 22	249
MEDLINE ALL	23/2/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to February 22, 2024	106

Search strategy history

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

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

Searches
mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, staphylococcal"] or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 4393
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15537
#3 #1 or #2 16778
#4 (High* NEAR/1 (flow* or frequency*) NEAR/4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)):ti,ab 2846
#5 ((highflow* or higherflow* or HF) NEAR/4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)):ti,ab 2263
#6 (HFNC or HFNCT or HHHFNC or HFFM or HFNP):ti,ab 903
#7 {or #4-#6} 3753
#8 #3 and #7 350
#9 [mh ^Infant] or [mh ^"Infant Health"] or [mh ^"Infant Welfare"] or [mh ^"Infant Care"] 31147
#10 (infan* or baby* or babies or toddler* or (pre NEXT school*) or preschool* or kindergar*):ti,ab 61322
#11 [mh Child] or [mh "Child Behavior"] or [mh ^"Child Health"] or [mh ^"Child Welfare"] or [mh ^"Child Care"] 82051
#12 [mh ^Minors] 15
#13 (child* or minor or minors or boy* or girl* or kid or kids):ti,ab 185856
#14 [mh "pediatrics"] 1042
#15 (pediatric* or paediatric*):ti,ab 41469
#16 [mh ^Adolescent] or [mh ^"Adolescent Behavior"] or [mh ^"Adolescent Health"] or [mh ^Puberty] 136393
#17 ((under NEXT 18*) or (under NEXT eighteen*)):ti,ab 16861
#18 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or (school NEXT age*) or schoolage* or underage* or (under NEXT age*)):ti,ab 51067
#19 (young* NEAR/1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)):ti,ab 29322
#20 {or #9-#19} 391048
#21 #8 and #20 89
#22 ((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an 494409
#23 #21 not #22 35
#24 "conference":pt 236547
#25 #23 not #24 24
#26 #23 not #24 in Trials 22

Database name: Embase

Searches
1 pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or

Searches
neonatal pneumonia/ or obstructive pneumonia/ or organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ or hospital acquired pneumonia/ 319791
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 237264
3 1 or 2 403008
4 high flow nasal cannula therapy/ 6186
5 humidified high flow nasal cannula therapy/ 186
6 (High* adj1 (flow* or frequency*) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 10663
7 ((highflow* or higherflow* or HF) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 5948
8 (HFNC or HFNCT or HHHFNC or HFFM or HFNP).ti,ab. 2565
9 or/4-8 19732
10 3 and 9 2878
11 Juvenile/ or exp child/ or child health/ or infant welfare/ or Child Behavior/ or Child Welfare/ or exp child care/ or "minor (person)"/ 3245931
12 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 737398
13 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2658767
14 exp pediatrics/ 129368
15 (pediatric* or paediatric*).ti,ab. 729689
16 exp adolescent/ or adolescent behavior/ or adolescent health/ or exp Puberty/ 1853038
17 elementary student/ or high school student/ or middle school student/ 13476
18 ("under 18*" or "under eighteen*").ti,ab. 7795
19 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or "school age*" or schoolage* or underage* or "under age*").ti,ab. 784318
20 (young* adj1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)).ti,ab. 476598
21 or/11-20 5618945
22 10 and 21 634
23 limit 22 to english language 623
24 (letter or editorial).pt. 2104366
25 23 not 24 600
26 Case report/ 2969074
27 25 not 26 373
28 nonhuman/ not human/ 5386407
29 27 not 28 370
30 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5844635
31 29 not 30 249

Database name: MEDLINE ALL

Searches
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or healthcare-associated pneumonia/ 124812
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 161695
3 1 or 2 231640
4 (High* adj1 (flow* or frequency*) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 6176
5 ((highflow* or higherflow* or HF) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 3026
6 (HFNC or HFNCT or HHHFNC or HFFM or HFNP).ti,ab. 1379
7 or/4-6 9195
8 3 and 7 743
9 Infant/ or Infant Health/ or Infant Welfare/ or Infant Care/ 883027
10 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 619684
11 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ or Child Care/ 2198428
12 Minors/ 2844
13 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2081876
14 exp pediatrics/ 63255
15 (pediatric* or paediatric*).ti,ab. 463144
16 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ or Puberty/ 2241155
17 ("under 18*" or "under eighteen*").ti,ab. 4427
18 (adolescen* or pubescen* or prepubescen* or puberty* or prepubert* or teen* or preteen* or juvenil* or youth* or youngster* or schoolchild* or "school age*" or schoolage* or underage* or "under age*").ti,ab. 612402
19 (young* adj1 (adult* or person* or people* or men or man or women* or woman* or male* or female* or patient* or inpatient* or outpatient*)).ti,ab. 348363
20 or/9-19 5020329
21 8 and 20 141
22 limit 21 to english language 129
23 limit 22 to (letter or historical article or comment or editorial or news or case reports) 23
24 22 not 23 106
25 Animals/ not (Animals/ and Humans/) 5164074
26 24 not 25 106

Part 2C: Effectiveness evidence searches (adults, children and young people) – cohort studies

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	2/7/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 6 of 12, June 2024	172
Embase	2/7/2024	Ovid	Embase 1974 to 2024 July 01	2697
MEDLINE ALL	2/7/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to July 01, 2024	1266

Search strategy history

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

Searches	
#1	[mh ^pneumonia] or [mh ^bronchopneumonia] or [mh ^pleuropneumonia] or [mh ^"pneumonia, bacterial"] or [mh ^"chlamydial pneumonia"] or [mh ^"pneumonia, mycoplasma"] or [mh ^"pneumonia, pneumococcal"] or [mh ^"pneumonia, staphylococcal"] or [mh ^"pneumonia, necrotizing"] or [mh ^"pneumonia, viral"] or [mh ^"organizing pneumonia"] or [mh ^"healthcare-associated pneumonia"] 4441
#2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 16100
#3	#1 or #2 17344
#4	[mh "positive-pressure respiration"] 4186
#5	[mh ^"non-invasive ventilation"] 568
#6	((non-invasive* or (non NEXT invasive*) or (positive NEXT pressure*) or (pressure NEXT release*) or helmet*) NEAR/3 (respir* or breath* or ventilat* or airway*)):ti,ab 6088
#7	(((positive NEXT airway*) or (continuous NEXT distend*) or ("positive end" NEXT expiratory*)) NEAR/1 pressur*):ti,ab 7255
#8	(CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP):ti,ab 10959
#9	(High* NEAR/1 (flow* or frequency*) NEAR/4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)):ti,ab 3016
#10	((highflow* or higherflow* or HF) NEAR/4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)):ti,ab 2414
#11	(HFNC or HFNCT or HHHFNC or HFFM or HFNP):ti,ab 961
#12	{or #4-#11} 18659
#13	#3 and #12 1102
#14	[mh "Cohort studies"] 211770

Searches
#15 ((follow-up* or followup* or concurrent* or incidence* or population*) NEAR/3 (study* or studies* or analy* or observation* or design* or method* or research*)):ti,ab 75024
#16 (longitudinal* or prospective* or retrospective* or cohort*):ti,ab 332064
#17 [mh ^"epidemiologic methods"] with Publication Year from 1970 to 1989, in Trials 58
#18 {or #14-#17} 470354
#19 #13 and #18 341
#20 ((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an 524201
#21 #19 not #20 239
#22 "conference":pt 245616
#23 #21 not #22 176
#24 #21 not #22 in Trials 172

Database name: Embase

Searches
1 pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ or hospital acquired pneumonia/ 327453
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 242862
3 1 or 2 412281
4 positive pressure ventilation/ or exp continuous positive airway pressure/ or exp intermittent positive pressure ventilation/ or exp non-invasive positive pressure ventilation/ or exp positive end expiratory pressure ventilation/ or exp helmet ventilation/ 26029
5 non-invasive ventilation/ 21404
6 ((non-invasive* or "non invasive*" or "positive pressure*" or "pressure release*" or helmet*) adj3 (respir* or breath* or ventilat* or airway*)).ti,ab. 33562
7 (("positive airway*" or "continuous distend*" or "positive end expiratory*") adj1 pressur*).ti,ab. 31425
8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP).ti,ab. 52420
9 high flow nasal cannula therapy/ 6845
10 humidified high flow nasal cannula therapy/ 198
11 (High* adj1 (flow* or frequency*) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 11244
12 ((highflow* or higherflow* or HF) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 6160
13 (HFNC or HFNCT or HHHFNC or HFFM or HFNP).ti,ab. 2733

Searches
14 or/4-13 117171
15 3 and 14 11809
16 cohort analysis/ 1184799
17 longitudinal study/ 216207
18 prospective study/ 925178
19 retrospective study/ 1642594
20 follow up/ 2211193
21 ((follow up* or followup* or concurrent* or incidence* or population*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. 853225
22 (longitudinal* or prospective* or retrospective* or cohort*).ti,ab. 4352217
23 or/16-22 6487701
24 15 and 23 5211
25 limit 24 to english language 5079
26 (letter or editorial).pt. 2139309
27 25 not 26 4969
28 Case report/ 3014736
29 27 not 28 4222
30 nonhuman/ not human/ 5474544
31 29 not 30 4180
32 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5986621
33 31 not 32 2697

Database name: MEDLINE ALL

Searches
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or healthcare-associated pneumonia/ 125658
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 164694
3 1 or 2 234813
4 exp positive-pressure respiration/ 29808
5 non-invasive ventilation/ 3913
6 ((non-invasive* or "non invasive*" or "positive pressure*" or "pressure release*" or helmet*) adj3 (respir* or breath* or ventilat* or airway*)).ti,ab. 20496
7 (("positive airway*" or "continuous distend*" or "positive end expiratory*") adj1 pressur*).ti,ab. 21526
8 (CPAP or AUTOPAP or AUTOCPAP or "AUTO PAP" or APRV or NCPAP or NPPV or NIPPV or BIPAP or VPAP or APAP or ACPAP or NIV or PEEP or BCPAP or BPAP or IPPV or FCPAP or HCPAP).ti,ab. 28402
9 (High* adj1 (flow* or frequency*) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 6428
10 ((highflow* or higherflow* or HF) adj4 (cannula* or canula* or oxygen* or therap* or nasal* or nose* or prong* or mask* or respirator* or insufflat*)).ti,ab. 3158
11 (HFNC or HFNCT or HHHFNC or HFFM or HFNP).ti,ab. 1465
12 or/4-11 66948

Searches		
13	3 and 12	3666
14	exp Cohort studies/	2623262
15	((follow up* or followup* or concurrent* or incidence* or population*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab.	507133
16	(longitudinal* or prospective* or retrospective* or cohort*).ti,ab.	2747647
17	epidemiologic methods/ and (197* or 198*).yr.	10282
18	or/14-17	4011764
19	13 and 18	1441
20	Animals/ not (Animals/ and Humans/)	5202533
21	19 not 20	1432
22	limit 21 to english language	1325
23	limit 22 to (letter or historical article or comment or editorial or news or case reports)	59
24	22 not 23	1266

Part 3: Cost effectiveness searches

Database results

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

Re-run results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Econlit	14/10/2024	Ovid	Econlit 1886 to October 03, 2024	6

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

Search strategy history

Database name: Econlit

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

Database name: Embase

Searches	
1	pneumonia/ or bilateral pneumonia/ or bronchopneumonia/ or granulomatous pneumonia/ or infectious pneumonia/ or interstitial pneumonia/ or necrotizing pneumonia/ or neonatal pneumonia/ or obstructive pneumonia/ or exp organizing pneumonia/ or bacterial pneumonia/ or community acquired pneumonia/ or health care associated pneumonia/ or hospital acquired pneumonia/ or exp lobar pneumonia/ or virus pneumonia/ or chlamydial pneumonia/ or escherichia coli pneumonia/ or haemophilus influenzae pneumonia/ or pulmonary nocardiosis/ or mycoplasma pneumonia/ or rickettsial pneumonia/ or exp staphylococcal pneumonia/ or exp streptococcus pneumonia/ 314875
2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 232562
3	1 or 2 395881
4	cost utility analysis/ 12471
5	quality adjusted life year/ 35716
6	cost*.ti. 195365
7	(cost* adj2 utilit*).tw. 12784
8	(cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw.385741
9	(economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 66452
10	(qualit* adj2 adjust* adj2 life*).tw. 27335
11	QALY*.tw. 26801
12	(incremental* adj2 cost*).tw. 28720

Searches
13 ICER.tw. 13032
14 utilities.tw. 15135
15 markov*.tw. 40152
16 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. 72706
17 ((utility or effective*) adj2 analys*).tw. 37800
18 (willing* adj2 pay*).tw. 14735
19 (EQ5D* or EQ-5D*).tw. 26137
20 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 5262
21 (european* adj2 quality adj3 ("5" or five)).tw. 996
22 or/4-21 635358
23 3 and 22 7788
24 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ 1716014
25 exp "organisation for economic co-operation and development"/ 2774
26 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ 3801223
27 european union/ 31487
28 developed country/ 35727

Searches		
29	or/25-28	3834983
30	24 not 29	1561961
31	23 not 30	6971
32	limit 31 to english language	6647
33	(letter or editorial).pt.	2081948
34	32 not 33	6549
35	Case report/	2939178
36	34 not 35	6182
37	nonhuman/ not human/	5325269
38	36 not 37	6027
39	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.	5742113
40	38 not 39	4181
41	limit 40 to yr="2014 -Current"	2288
Note: in the re-run Line 41 was changed to limit 40 to dc=20231101-20241014.		

Database name: International HTA Database

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

Database name: MEDLINE ALL

Searches		
1	pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, rickettsial/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or cryptogenic organizing pneumonia/ or healthcare-associated pneumonia/	125178
2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab.	159311
3	1 or 2	229286
4	Cost-Benefit Analysis/	93463
5	Quality-Adjusted Life Years/	15940
6	Markov Chains/	16047
7	exp Models, Economic/	16244
8	cost*.ti.	146284

Searches
9 (cost* adj2 utilit*).tw. 7812
10 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw.279720
11 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 47585
12 (qualit* adj2 adjust* adj2 life*).tw. 18059
13 QALY*.tw. 14611
14 (incremental* adj2 cost*).tw. 17628
15 ICER.tw. 6134
16 utilities.tw. 9537
17 markov*.tw. 32169
18 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw.54722
19 ((utility or effective*) adj2 analys*).tw. 25292
20 (willing* adj2 pay*).tw. 9954
21 (EQ5D* or EQ-5D*).tw. 13646
22 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 3930
23 (european* adj2 quality adj3 ("5" or five)).tw. 723
24 or/4-23 506237
25 3 and 24 3855
26 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ 1312779
27 "organisation for economic co-operation and development"/ 565
28 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or

Searches
israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ 3515662
29 european union/ 17814
30 developed countries/ 21444
31 or/27-30 3531767
32 26 not 31 1222696
33 25 not 32 3418
34 limit 33 to english language 3185
35 limit 34 to (letter or historical article or comment or editorial or news or case reports) 181
36 34 not 35 3004
37 Animals/ not (Animals/ and Humans/) 5137547
38 36 not 37 2921
39 limit 38 to yr="2014 -Current" 1534
Note: in the re-run the following lines were used:
38 36 not 37
39 limit 38 to ed=20231101-20241014
40 limit 38 to dt=20231101-20241014
41 39 or 40

Database name: NHS Economic Evaluation Database (NHS EED)

Searches
1 MeSH DESCRIPTOR Pneumonia 252
2 MeSH DESCRIPTOR bronchopneumonia 1
3 MeSH DESCRIPTOR pleuropneumonia 0
4 MeSH DESCRIPTOR pneumonia, bacterial 90
5 MeSH DESCRIPTOR chlamydial pneumonia 0
6 MeSH DESCRIPTOR pneumonia, mycoplasma 3
7 MeSH DESCRIPTOR pneumonia, pneumococcal 48
8 MeSH DESCRIPTOR pneumonia, rickettsial 0
9 MeSH DESCRIPTOR pneumonia, staphylococcal 10
10 MeSH DESCRIPTOR pneumonia, necrotizing 0
11 MeSH DESCRIPTOR pneumonia, viral 9
12 MeSH DESCRIPTOR Cryptogenic Organizing Pneumonia 0
13 MeSH DESCRIPTOR healthcare-associated pneumonia 0
14 (pneumonia) OR (pneumonias) 1118
15 (bronchopneumon*) OR (pleuropneumon*) 3
16 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 1120
17 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15) IN NHSEED 425

Searches
18 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15) IN NHSEED FROM 2014 TO 2024 11 Note: no re-run required as the database has been archived and not updated since 31 March 2015.

Appendix C – Effectiveness evidence study selection

Figure 1: RCT study selection for non-invasive ventilation in adults

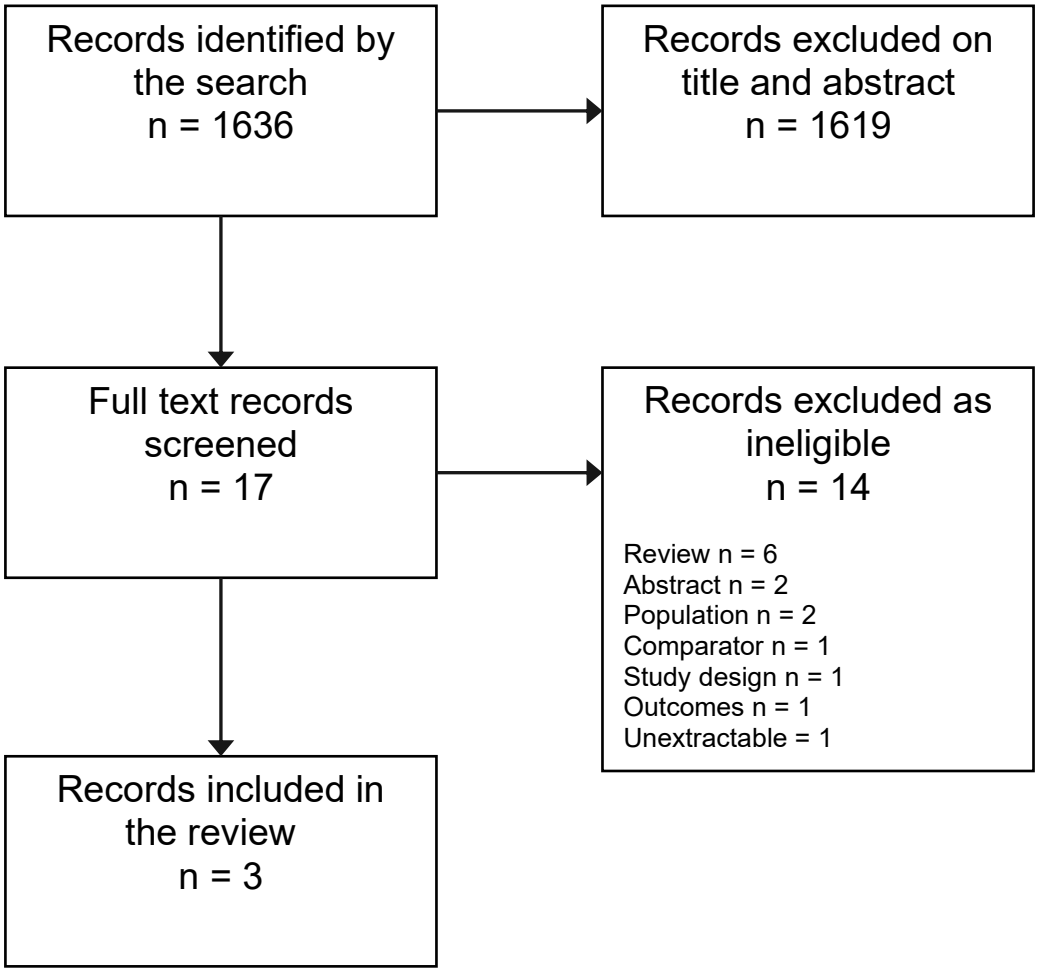


Figure 2: RCT study selection for non-invasive ventilation in babies, children and young people

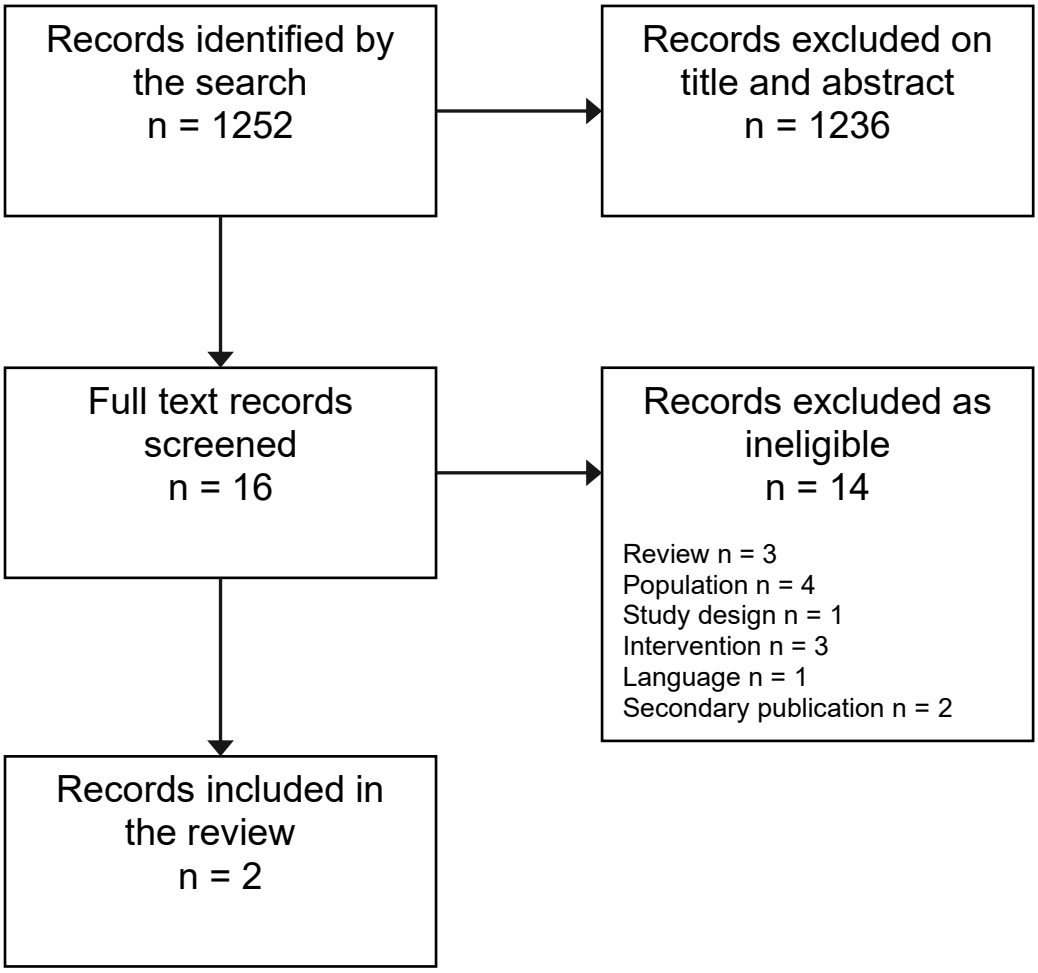
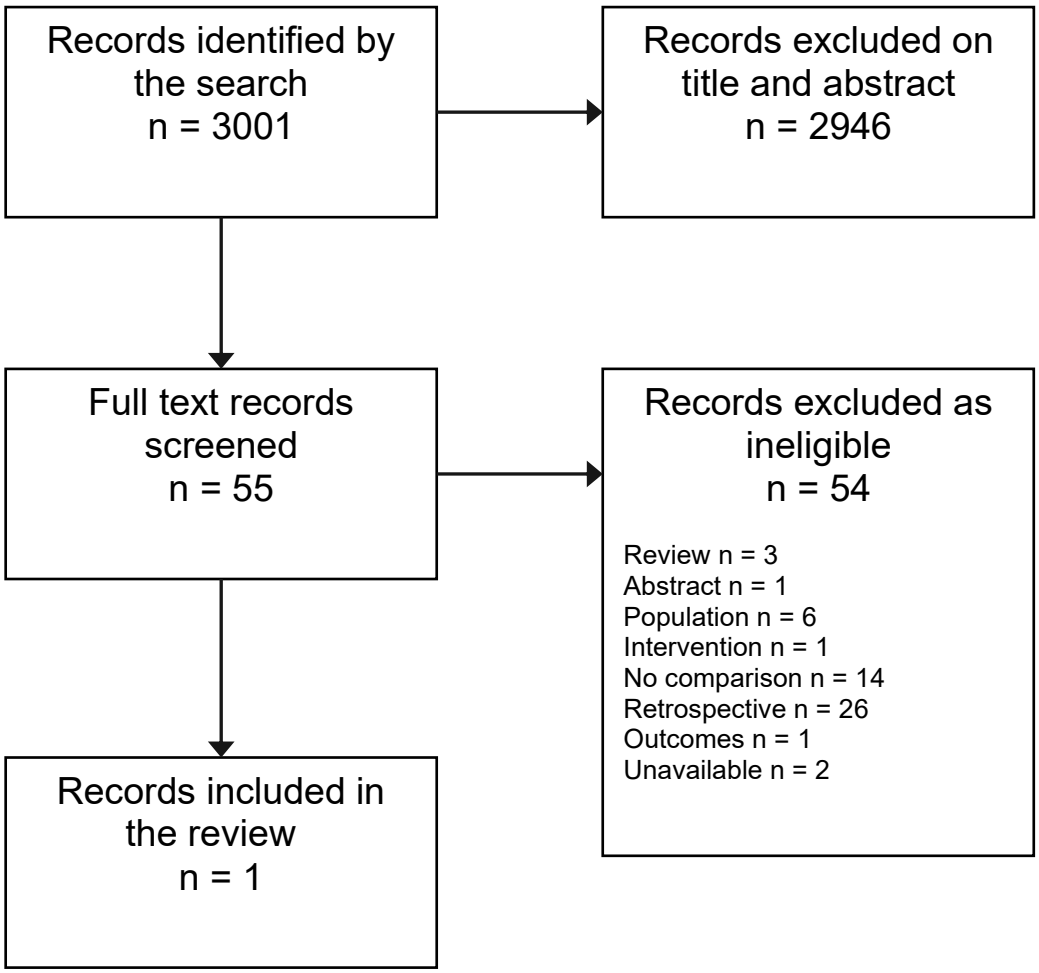


Figure 3: Prospective cohort study selection for non-invasive ventilation in adults, babies, children and young people



Appendix D – Effectiveness evidence

Brambilla, 2014

Bibliographic Reference	Brambilla, Anna Maria; Aliberti, Stefano; Prina, Elena; Nicoli, Francesco; Del Forno, Manuela; Nava, Stefano; Ferrari, Giovanni; Corradi, Francesco; Pelosi, Paolo; Bignamini, Angelo; Tarsia, Paolo; Cosentini, Roberto; Helmet CPAP vs. oxygen therapy in severe hypoxemic respiratory failure due to pneumonia.; Intensive care medicine; 2014; vol. 40 (no. 7); 942-9

Study details

Trial registration number and/or trial name	NCT01383213
Study type	Randomised controlled trial (RCT)
Study location	Italy
Study setting	high dependency units (HDU) of four Italian hospitals
Study dates	2011-2013
Sources of funding	University of Milan
Inclusion criteria	Aged over 18 men and women of any ethnic group dyspnoea at rest with respiratory rate (RR) ≥30 breath/min or sign of respiratory distress PaO2/FiO2 ratio≤250 evaluated during oxygen therapy supplied at least 1 hour through a Venturi mask with FiO2 ≥0,50 diagnosis of pneumonia as unique cause of severe acute respiratory failure
Exclusion criteria	diagnosis of other causes of severe acute respiratory failure unstable angina or acute myocardial infarction acute respiratory acidosis with pH <7,35 and PaCO2 >45 mmHg systolic BP <90 mmHg despite fluid resuscitation or vasopressors severe arrhythmias convulsions

	degree of consciousness, Kelly score>3 swallowing disturbance with increasing risk of aspiration pneumonia inability to protect the airway recent facial trauma or burn non-collaborative patient presence of open wounds (head, thorax, abdomen) respiratory arrest or need of intubation pregnancy or suspect of pregnancy
Intervention(s)	Helmet CPAP: treated with CPAP using a helmet, initial PEEP of 10 cmH20 and an FiO2 set in order to maintain SpO2 ≥92%.
Comparator	Oxygen therapy: treated with oxygen therapy by Venturi mask with an FiO2 set in order to maintain SpO2 ≥92%.
Outcome measures	Mortality Need for invasive mechanical ventilation Meeting the clinical criteria, but not necessarily being intubated. Duration of hospital stay Adverse events
Number of participants	A total of 81 patients were enrolled between February 2010 and February 2013: 40 patients randomized to CPAP and 41 to the control group.
Duration of follow-up	participants were followed for the duration of hospital stay
Loss to follow-up	No loss to follow up
Methods of analysis	Data were analysed according to the strict intent-to-treat approach, without replacement of missing data. Data were summarised as mean ± SD and compared by independent-samples t-test if normally distributed; as median ± range interquartile (IQR) and analysed with the Mann–Whitney U test if not normally distributed; and as frequency with proportion and analysed with Chi square or the Fisher's exact test as appropriate when nominal.
Additional comments	

Abbreviations:
CPAP: Continuous positive airway pressure
PEEP: Positive end-expiratory pressure

Study arms

CPAP (N = 40)

CPAP was delivered through a high-flow generator (90–140 L/min; VitalSigns Inc., Totowa, NJ) using a helmet (StarMed, Mirandola, Italy) as interface with initial positive end-expiratory pressure (PEEP) of 10 cmH2O and with an FiO2 set to maintain a pulse oximetry (SpO2) of at least 92 %, as previously reported

Standard oxygen therapy (N = 41)

Standard oxygen therapy was supplied through a Venturi mask with an FiO2 delivered to maintain an SpO2 of at least 92 %

Characteristics

Arm-level characteristics

Characteristic	CPAP (N = 40)	Standard oxygen therapy (N = 41)
% Female Nominal	40	29.3
Mean age (SD) Mean (SD)	64.9 (16.1)	69.5 (15.8)
Smoking status (%) Nominal	42.5	53.7
PSI risk class IV-V Nominal	82.5	82.9
CURB 65 score >=3 Nominal	47.5	51.2
CVD Nominal	42.5	51.2
COPD Nominal	7.5	19.5
Diabetes Nominal	20	14.6
Chronic renal failure Nominal	17.5	17.1
Solid neoplasia Nominal	5	12.2

Characteristic	CPAP (N = 40)	Standard oxygen therapy (N = 41)
Hematologic neoplasia Nominal	7.5	7.3
Immunosuppression Nominal	20	12.2

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

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

Frat, 2019

Bibliographic Reference	Frat, Jean-Pierre; Ricard, Jean-Damien; Quenot, Jean-Pierre; Pichon, Nicolas; Demoule, Alexandre; Forel, Jean-Marie; Mira, Jean-Paul; Coudroy, Remi; Berquier, Guillaume; Voisin, Benoit; Colin, Gwenhael; Pons, Bertrand; Danin, Pierre Eric; Devaquet, Jerome; Prat, Gwenael; Clere-Jehl, Raphael; Petitpas, Franck; Vivier, Emmanuel; Razazi, Keyvan; Nay, Mai-Anh; Souday, Vincent; Dellamonica, Jean; Argaud, Laurent; Ehrmann, Stephan; Gibelin, Aude; Girault, Christophe; Andreu, Pascal; Vignon, Philippe; Dangers, Laurence; Ragot, Stephanie; Thille, Arnaud W; Non-invasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation of patients with acute hypoxaemic respiratory failure: a randomised, multicentre, open-label trial.; The Lancet. Respiratory medicine; 2019; vol. 7 (no. 4); 303-312

Study details

Trial registration number and/or trial name	NCT01320384
Study type	Randomised controlled trial (RCT)
Study location	France and Belgium.
Study setting	23 ICUs
Study dates	February 2011 to April 2013
Sources of funding	Programme Hospitalier de Recherche Clianique Interrégional 2010 of the French Ministry of Health
Inclusion criteria	Aged over 18 a respiratory rate of more than 25 breaths per minute a ratio of the partial pressure of arterial oxygen (Pao2) to the Fio2 of 300 mm Hg or less while the patient was breathing oxygen at a flow rate of 10 litres per minute or more for at least 15 minute a partial pressure of arterial carbon dioxide (Paco2) not higher than 45 mm Hg an absence of clinical history of underlying chronic respiratory failure
Exclusion criteria	Paco2 of more than 45 mm Hg exacerbation of asthma or chronic respiratory failure cardiogenic pulmonary oedema severe neutropenia

	haemodynamic instability use of vasopressors a Glasgow Coma Scale score of 12 points or less contraindications to non-invasive ventilation a do-not-intubate order
Intervention(s)	In the high-flow–oxygen group, oxygen was passed through a heated humidifier (MR850, Fisher and Paykel Healthcare) and applied continuously through large-bore binasal prongs, with a gas flow rate of 50 litres per minute and an Fio2 of 1.0 at initiation (Optiflow, Fisher and Paykel Healthcare). The fraction of oxygen in the gas flowing in the system was subsequently adjusted to maintain an Spo2 of 92% or more. High-flow oxygen was applied for at least 2 calendar days; it could then be stopped and the patient switched to standard oxygen therapy. In the non-invasive-ventilation group, non-invasive ventilation was delivered to the patient through a face mask (Fisher and Paykel Health care) that was connected to an ICU ventilator, with pressure support applied in a non-invasive ventilation mode. The pressure-support level was adjusted with the aim of obtaining an expired tidal volume of 7 to 10 ml per kilogram of predicted body weight, with an initial positive end expiratory pressure (PEEP) between 2 and 10 cm of water. The Fio2 or PEEP level (or both) were then adjusted to maintain an Spo2 of 92% or more. The minimally required duration of non invasive ventilation was 8 hours per day for at least 2 calendar days. Non-invasive ventilation was applied during sessions of at least 1 hour and could be resumed if the respiratory rate was more than 25 breaths per minute or the Spo2 was less than 92%. Between non-invasive-ventilation sessions, patients received high-flow oxygen, as described above.
Comparator	In the standard-oxygen group, oxygen therapy was applied continuously through a nonrebreather face mask at a flow rate of 10 litres per minute or more. The rate was adjusted to maintain an oxyagen saturation level of 92% or more, as measured by means of pulse oximetry (Spo2), until the patient recovered or was intubated.
Outcome measures	Mortality Need for invasive mechanical ventilation Duration of hospital stay Complications (empyema, effusion, abscess, metastatic infection, superinfection, MODS, pneumothorax)
Number of participants	2506 patients with acute hypoxemic respiratory failure were admitted to the 23 participating ICUs; 525 patients were eligible for inclusion in the study,

	and 313 underwent randomization (Fig. 1). After the secondary exclusion of 3 patients who withdrew consent, 310 patients were included in the analysis. A total of 94 patients were assigned to standard oxygen therapy, 106 to high-flow oxygen therapy, and 110 to non-invasive ventilation
Duration of follow-up	**90 days**
Loss to follow-up	310 Were included in the analysis and in the 90-day follow-up 106 Were in the high-flow–oxygen group 94 Were in the standard-oxygen group 110 Were in the non-invasive-ventilation group.
Methods of analysis	All the analyses were performed on an intention-to-treat basis. Variables associated with intubation at day 28 and in-ICU mortality were assessed by means of multivariate logistic-regression analyses, and those associated with mortality at 90 days were assessed by means of a Cox proportional-hazard regression analysis with the use of a backward-selection procedure.

Abbreviations:
PEEP: Positive end-expiratory pressure
MODS: Multiple organ dysfunction syndrome

Study arms

high flow nasal oxygen (N = 106)

high flow nasal of humidified oxygen, set between 30 to 50 l/min. The inspired fraction of oxygen (FiO2) will be adjusted in order to obtain a SpO2 >92%.

non-invasive-ventilation (N = 110)

The pressure-support level was adjusted with the aim of obtaining an expired tidal volume of 7 to 10 ml per kilogram of predicted body weight, with an initial positive end expiratory pressure (PEEP) between 2 and 10 cm of water. The Fio2 or PEEP level (or both) were then adjusted to maintain an Spo2 of 92% or more

standard oxygen (N = 94)

oxygen therapy was applied continuously through a nonrebreather face mask at a flow rate of 10 litres per minute or more. The rate was adjusted to maintain an oxygen saturation level of 92% or more.

Characteristics

Arm-level characteristics

Characteristic	high flow nasal oxygen (N = 106)	non-invasive-ventilation (N = 110)	standard oxygen (N = 94)
% Female Nominal	29	33	33
Mean age (SD) Mean (SD)	61 (16)	61 (17)	59 (17)
Smoking status (%) Nominal	32	36	38

Characteristic	high flow nasal oxygen (N = 106)	non-invasive-ventilation (N = 110)	standard oxygen (N = 94)
BMI Mean (SD)	25 (5)	26 (6)	26 (5)
CAP Nominal	67	63	61
HAP Nominal	11	11	14
Immunosuppression Nominal	6	9	4
Non-pneumonia Nominal	16	17	21

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

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Indirectly applicable *(Study did not aim to examine patients with pneumonia specifically, but the majority of the included sample fit the profile of this review)*

He, 2019

Bibliographic Reference	He, Hangyong; Sun, Bing; Liang, Lirong; Li, Yanming; Wang, He; Wei, Luqing; Li, Guofeng; Guo, Shuliang; Duan, Jun; Li, Yuping; Zhou, Ying; Chen, Yusheng; Li, Hongru; Yang, Jingping; Xu, Xiyuan; Song, Liqiang; Chen, Jie; Bao, Yong; Chen, Feng; Wang, Ping; Ji, Lixi; Zhang, Yongxiang; Ding, Yanyan; Chen, Liangan; Wang, Ying; Yang, Lan; Yang, Tian; Weng, Heng; Li, Hongyan; Wang, Daoxin; Tong, Jin; Sun, Yongchang; Li, Ran; Jin, Faguang; Li, Chunmei; He, Bei; Sun, Lina; Wang, Changzheng; Hu, Mingdong; Yang, Xiaohong; Luo, Qin; Zhang, Jin; Tan, Hai; Wang, Chen; A multicenter RCT of non-invasive ventilation in pneumonia-induced early mild acute respiratory distress syndrome.; Critical care (London, England); 2019; vol. 23 (no. 1); 300

Study details

Trial registration number and/or trial name	NCT01581229
Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	21 departments of respiratory and critical care medicine of 21 university-affiliated hospitals across 10 provinces in Mainland China
Study dates	June 2012 - December 2016
Sources of funding	Beijing Hospital
Inclusion criteria	Aged over 18 a clinical presentation of respiratory distress; acute onset Arterial oxygen tension/inspired oxygen fraction (PaO2/FIO2) < 300 mmHg but > 200 mmHg while breathing oxygen delivered by a conventional Venturi device at a maximum concentration (50%); presence of bilateral pulmonary infiltrates on posteroanterior chest radiograph the cause of ALI is considered to be intro-pulmonary no evidence of left heart failure as assessed by echocardiography and/or a pulmonary artery wedge pressure of <18 mm Hg.
Exclusion criteria	severe arrhythmias inability to protect the airway recent facial trauma or burn to airway non-collaborative patient

	Refusal Glasgow Coma Scale < 11 pneumothorax or pneumomediastinum; cardiogenic shock or severe hemodynamic instability (systolic blood pressure <90 mmHg associated with decreased urinary output (<20 mL.h-1) despite fluid repletion and use of vasoactive agents) of other causes severe organ dysfunction (Sequential Organ Failure Assessment score > 3 end-stage patients who were expected to survive < 6 months severe abdominal distension the cause of ALI is considered to be extrapulmonary active upper gastrointestinal bleeding
Intervention(s)	non-invasive positive pressure ventilation: Patients in the NPPV group are ventilated using the CPAP or bilevel positive airways pressure S/T mode. NIV was delivered for no less than 16 h a day in the first 3 days after entry into the study.
Comparator	oxygen therapy: In the control group, Venturi masks are used to maintain SpO2 at 92% to 96% by adjusting the oxygen flow rates.
Outcome measures	Mortality Need for invasive mechanical ventilation Number who met intubation criteria and the number intubated Duration of hospital stay
Number of participants	204 patients were enrolled. 105 were allocated to the NIV group and 99 to the control group. 200 patients were included in the final analysis.
Duration of follow-up	1 year
Loss to follow-up	4 excluded during the treatment phase: Three patients refused NIV after randomization to the NIV group, and 1 patient was diagnosed as having tuberculosis in the control group
Methods of analysis	Quantitative continuous variables were given as either means (± SDs) or medians (with inter-quartile ranges) that were compared using the unpaired Student’s t test or the Mann-Whitney test. Qualitative or categorical variables were compared with the chi-square test or Fisher’s exact test. ANOVA for paired tests to

	compare the same variables collected at different time points was used.

Abbreviations:
CPAP: Continuous positive airway pressure
NPPV: Non-invasive positive pressure ventilation
NIV: Non-invasive ventillation
ALI: Acute lung injury

Study arms

Non-invasive ventilation (N = 102)

Patients in the NIV group were ventilated using the bilevel positive airway pressure S/T mode (BiPAP)

Conventional oxygen therapy (N = 98)

In the control group, Venturi masks were used to maintain SpO2 at 92 to 96% by adjusting the oxygen flow rates and FIO2

Characteristics

Arm-level characteristics

Characteristic	Non-invasive ventilation (N = 102)	Conventional oxygen therapy (N = 98)
% Female Nominal	33.2	35.8
Mean age (SD) Mean (SD)	53 (18.2)	56 (17.5)
Smoking status (%) Nominal	33.3	25.5
BMI Mean (SD)	22.4 (3.2)	22.3 (4.5)
APACHE II score Mean (SD)	7 (4.3)	8.1 (4.2)
Hypertension Nominal	24.5	23.5
Diabetes Nominal	6.9	18.4
Coronary heart disease Nominal	5.9	5.1

Characteristic	Non-invasive ventilation (N = 102)	Conventional oxygen therapy (N = 98)
Chronic heart failure Nominal	1	2
Chronic renal insufficiency Nominal	3.9	8.2
Cancer Nominal	3.9	2
Cerebrovascular disease Nominal	2	7.1
Immunosuppression Nominal	8.8	10.2
HAP Nominal	6.9	5.1
CAP Nominal	93.1	94.9

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

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

Liu, 2020

Bibliographic Reference	Liu, Cong; Cheng, Wei Yu; Li, Jun Shao; Tang, Tian; Tan, Ping Li; Yang, Lin; High-Flow Nasal Cannula vs. Continuous Positive Airway Pressure Therapy for the Treatment of Children <2 Years With Mild to Moderate Respiratory Failure Due to Pneumonia.; Frontiers in pediatrics; 2020; vol. 8; 590906

Study details

Trial registration number and/or trial name	ChiCTR2000030463
Study type	Randomised controlled trial (RCT)
Study location	Chongqing, China.
Study setting	emergency ward of Children's Hospital Affiliated to Chongqing Medical University
Study dates	between January 2018 and December 2019
Sources of funding	Chongqing Health Committee of China
Inclusion criteria	Under 2 years old severe pneumonia no indication of emergency tracheal intubation relatively stable vital signs under traditional oxygen inhalation. Mild to moderate respiratory failure defined by hypoxemia level of 150 <oxygenation index (PaO_2/FiO_2 ratio) < 300 and $PaCO_2$ <70 mm Hg with spontaneous breathing under standard oxygen
Exclusion criteria	patients with complicated congenital heart disease, severe malnutrition, neuromuscular disease, metabolic disease, and other serious basic diseases patients with chronic lung disease, secondary respiratory failure, including bronchopulmonary dysplasia, congenital airway dysplasia, and other chronic lung diseases patients who stopped treatment in the middle
Intervention(s)	The CPAP group: the initial parameter was set at 50–60% oxygen concentration, the pressure was set at 4–6 cm H_2O, and the flow rate of oxygen supply was set at 5–10 L/min to maintain the transcutaneous oxygen saturation ≥92–94%.
Comparator	The HFNC group: patients received Airvo2 type warm humidification high flow double chamber nasal oxygen therapy ventilator (Fisher Parker company of New Zealand) for ventilation within 3 h. The initial parameter

	was set at 50-60% oxygen concentration, and the inhaled oxygen flow was set at 2 L/kg/min to a limit of 20 L/min to maintain the transcutaneous oxygen saturation ≥92–94%.
Outcome measures	mortality intubation duration of hospital stay Adverse events
Number of participants	During the study period, a total of 155 infants aged <2 years were hospitalized for pneumonia with respiratory failure. A total of 71 children were excluded. Thus, 84 children were included in the analysis, with 43 assigned to each condition.
Duration of follow-up	Unspecified
Loss to follow-up	2 from CPAP group: parents declined CPAP.
Methods of analysis	For group comparisons, according to the normal distribution, the measurement data were represented by median (interquartile range) or mean ± standard deviation, and Wilcoxon rank-sum test or two-sided Student's t-test was used for non-normally distributed data and normally distributed data, respectively. Count data were represented by rate, and Chi^2 test was used for binary outcomes

Abbreviations:
CPAP: Continuous positive airway pressure
HFNC: High flow nasal canula

Study arms

nCPAP (N = 43)

nasal CPAP the initial parameter was set at 50–60% oxygen concentration, the pressure was set at 4–6 cm H2O, and the flow rate of oxygen supply was set at 5–10 L/min to maintain the transcutaneous oxygen saturation ≥92–94%.

HFNC (N = 43)

The HFNC group: patients received Airvo2 type warm humidification high flow double chamber nasal oxygen therapy ventilator (Fisher Parker company of New Zealand) for ventilation within 3 h. The initial parameter was set at 50-60% oxygen concentration, and the inhaled oxygen flow was set at 2 L/kg/min to a limit of 20 L/min to maintain the transcutaneous oxygen saturation ≥92–94%

Characteristics

Arm-level characteristics

Characteristic	nCPAP (N = 43)	HFNC (N = 43)
% Female (%) Nominal	43	44

Characteristic	nCPAP (N = 43)	HFNC (N = 43)
Age (Months) Median (IQR)	4 (1 to 11)	3 (2 to 11)
Comorbidities (%) Nominal	17	12
Weight (kg) Median (IQR)	6.5 (4.5 to 9.25)	6 (5 to 9)

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

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Indirectly applicable *(No control group comparator)*

Maitland, 2021

Bibliographic Reference	Maitland, K Kiguli, S Olupot-Olupot, P Hamaluba, M Thomas, K Alaroker, F Opoka, RO Tagoola, A Bandika, V Mpoya, A Mnjella, H Nabawanuka, E Okiror, W Nakuya, M Aromut, D Engoru, C Oguda, E Williams, TN Fraser, JF Harrison, DA Rowan, K; Randomised controlled trial of oxygen therapy and high-flow nasal therapy in African children with pneumonia; INTENSIVE CARE MEDICINE; 2021; vol. 47 (no. 5); 566 - 576

Study details

Trial registration number and/or trial name	ISRCTN Registry (ISRCTN15622505).
Study type	Randomised controlled trial (RCT)
Study location	Kenya and Uganda
Study setting	6 hospitals in low resource settings
Study dates	14th Feb 2017 to 28th Feb 2020
Sources of funding	The UK Joint Global Health Trials scheme: Medical Research Council, Foreign Commonwealth and Department Office, Department of Health and Social Care through the National Institute for Health Research and Wellcome Trust
Inclusion criteria	Children aged 28 days to 12 years hospitalised with a history of respiratory illness and any one of the 2013 WHO clinical definitions of severe pneumonia [13] plus hypoxaemia (SpO2<92%)
Exclusion criteria	previous diagnosed but uncorrected cyanotic heart disease, chronic lung disease (excluding asthma) children given oxygen given at another health facility (or>3 h at the current hospital) previous COAST enrolment
Intervention(s)	HFNT was delivered by AIRVO™2 device (https://www. fphcare.com/), which contains a humidifier with integrated flow generator that delivers, to spontaneous breathing patients, high flow warmed and humidified air/ oxygen blend. HFNT was initiated on FiO2 of 21% (room air) with flow rates increase and oxygen titrated in using a structured protocol. Reliable sources of oxygen including electricity power-back up for the AIRVO™2 and oxygen concentrators were provided to ensure oxygen delivery was uninterrupted
Comparator	LFO was delivered by nasal canulae/prongs and escalated to higher flow rates delivered by standard masks. Saturations were checked at 15-, 30-, and 60-min post-enrolment and during the structured reviews.
Outcome measures	Mortality at 28 days

	duration of hospital stay Adverse events hospital readmission
Number of participants	1842 eligible children were enrolled into the COAST trial and included in all analyses . Of 388 in the severe hypoxaemia stratum, 194 children were randomised to HFNT and 194 to LFO. Of 1454 children in the non-severe hypoxaemia stratum, 363 to were randomised to HFNT, 364 to LFO and 727 to permissive hypoxaemia.
Duration of follow-up	28 days
Loss to follow-up	Severe hypoxaemia HFNC: 194/194 Severe hypoxaemia standard oxygen: 192/194 Non-severe hypoxaemia HFNC: 362/363 Non-severe hypoxaemia standard oxygen: 362/364
Methods of analysis	Patients were analysed following a prespecified statistical analysis plan. The primary outcome was analysed as a binary outcome using multilevel logistic regression including both treatment allocation variables simultaneously.
Additional comments	COAST contained another study arm, permissive hypoxaemia, in which patients were only given low flow oxygen if SpO2 fell below 80%. This arm was not included in this review because it did not reflect UK practice and because the trial was stopped prematurely due to ethical objections to permissive hypoxaemia.

Abbreviations:
HFNT: High flow nasal therapy, otherwise known as high flow nasal canula

Study arms

HFNC - severe (N = 194)
high-flow nasal oxygen therapy in patients with severe hypoxaemia (SpO2<80%)

standard oxygen severe (N = 194)
standard oxygen therapy in patients with severe hypoxaemia (SpO2<80%)

HFNC non-severe (N = 363)
high-flow nasal oxygen therapy in patients with non-severe hypoxaemia (80 to<92%)

standard oxygen non-severe (N = 364)
standard oxygen therapy in patients with non-severe hypoxaemia (80 to<92%)

Characteristics

Arm-level characteristics

Characteristic	HFNC - severe (N = 194)	standard oxygen severe (N = 194)	HFNC non-severe (N = 363)	standard oxygen non-severe (N = 364)
% Female Nominal	52.1	50	41.3	41.2
Age (Months) Median (IQR)	7 (2 to 21)	7 (2 to 16)	9 (4 to 24)	9 (4 to 22)
Condition status (SpO2) Median (IQR)	75 (68 to 78)	75 (66 to 77)	88 (86 to 89)	88 (86 to 90)
Severely malnourished Nominal	9.8	14.9	2.8	6.6
sickle cell disease Nominal	5.2	3.6	7.2	7.1
developmental delay Nominal	8.3	8.2	5.8	4.7
severe anaemia Nominal	13	7.1	9.4	7.5
HIV Nominal	3.2	5.9	1.1	4.2
Malaria Nominal	13.4	9.9	14	10.8
Bacteraemia Nominal	5.3	3.8	2.3	2.3
Hypoglycaemia Nominal	5.2	4.7	1.9	1.4
Weight (kg) Median (IQR)	6.8 (4.8 to 10)	6.6 (4.8 to 9)	8.1 (6.4 to 111)	7.9 (6.2 to 10.4)

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

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Trial ended prematurely due to ethical problems with the interventions. The authors concluded that the COAST trial was unable answer the two specific hypotheses it was designed to address and was likely to be underpowered because of early termination.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Low resource setting is not comparable to UK healthcare, and clinical management in this setting is impacted by the resources available. Clinical profile of patients is also not comparable to UK population, with higher numbers of children with malaria, HIV, and malnourishment.)*

Brambilla, 2019

Bibliographic Reference	Brambilla, Anna Maria; Prina, Elena; Ferrari, Giovanni; Bozzano, Viviana; Ferrari, Rodolfo; Groff, Paolo; Petrelli, Giuseppina; Scala, Raffaele; Causin, Fabio; Noto, Paola; Bresciani, Emanuela; Voza, Antonio; Aliberti, Stefano; Cosentini, Roberto; Non-invasive positive pressure ventilation in pneumonia outside Intensive Care Unit: An Italian multicenter observational study.; European journal of internal medicine; 2019; vol. 59; 21-26

1.2 Study details

Secondary publication of another included study- see primary study for details	n/a
Other publications associated with this study included in review	n/a
Trial registration number and/or trial name	None
Study type	Prospective cohort study
Study location	Italy
Study setting	14 Emergency Departments (ERs) and 5 High Dependent Units (HDU)
Study dates	1st January 2013 to 31st December 2013
Sources of funding	None
Inclusion criteria	Over 18 years old Diagnosed pneumonia Acute respiratory failure Used either NIV or CPAP
Exclusion criteria	Admitted to ICU Initially treated with invasive mechanical ventilation
Intervention(s)	CPAP: continuous positive airway pressure set according to standard operating procedures at each centre.
Comparator	NPPV: non-invasive positive pressure ventilation set according to standard operating procedures at each centre.

Outcome measures	Mortality within 30 days Need for invasive mechanical ventilation
Number of participants	A total of 347 patients with ARF due to pneumonia. CPAP was applied in 176 (50.7%) and NPPV in 171 (49.3%) patients
Duration of follow-up	Within hospital stay
Loss to follow-up	None
Methods of analysis	The statistical analyses were performed using SPSS (version 20.0) for Mac (IBM, Armonk, NY, USA).The categorical data were presented as the number (percentage).The normally distributed data were presented as the mean (± SD) (or as median and interquartile range [IQR] for non-normally distributed data). Characteristics of patients treated with either CPAP or NPPV were compared. Categorical variables were compared with Chi-square and Fisher's exact tests. Quantitative continuous variables were compared using the Student t-test or the MannWhitney test for the normally and non-normally distributed variables, respectively. Independent risk factors for in-hospital mortality were analysed with a logistic regression analysis. A two-sided p-value of 0.05 or less was considered statistically significant.

Abbreviations:
CPAP: Continuous positive airway pressure
NPPV: Non-invasive positive pressure ventilation
NIV: Non-invasive ventilation
ARF: Acute respiratory failure

1.3 Study arms

1.3.1 CPAP (N = 176)

treated outside the ICU with continuous positive airway pressure (CPAP)

1.3.2 NPPV (N = 171)

treated outside the ICU with non-invasive positive pressure ventilation

1.4 Characteristics

1.4.1 Arm-level characteristics

Characteristic	CPAP (N = 176)	NPPV (N = 171)
% Female Nominal	38.6	45.6
Mean age (SD) Mean (SD)	72.42 (15)	75.18 (12)
CURB65>=3 Nominal	64	48

Characteristic	CPAP (N = 176)	NPPV (N = 171)
PSI >= IV Nominal	79	92
APACHE II score Mean (SD)	16.9 (5.9)	19.98 (5.3)
COPD Nominal	31.3	60.8
Congestive heart failure Nominal	14.8	31
Chronic kidney disease Nominal	26.1	25.1
Obesity Nominal	13.6	21.1
Neoplastic disease Nominal	22.7	19.8
CAP Nominal	84.1	86.5
HAP Nominal	15.3	12.9
Do not intubate order (%) Nominal	27.8	31.6

1.4.2 Critical appraisal - GDT Crit App - ROBINS-I: a tool for non-randomised studies of interventions

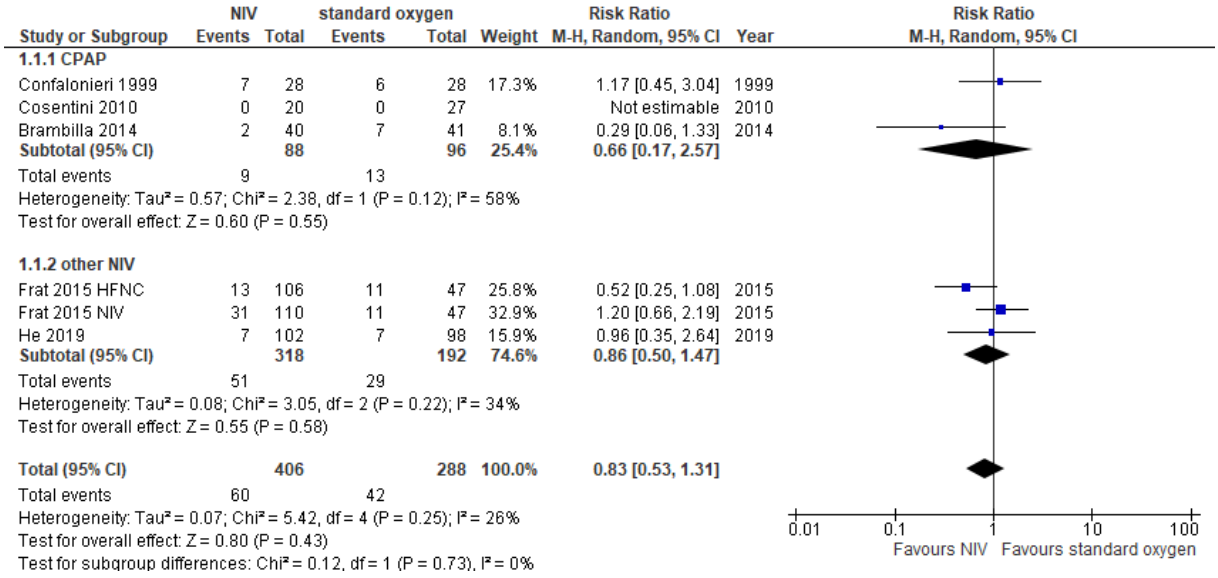
Section	Question	Answer
Overall bias	Risk of bias judgement	Low
Overall bias	Directness	Indirectly Applicable *(No control group, only NIV)*

Appendix E – Forest plots

1.4.3 RCTs of non-invasive ventilation vs standard oxygen in adults

Figure 1: Mortality: Number of patients who had died at follow-up under 30 days.

Lower scores favour non-invasive ventilation.



Abbreviations:
CPAP: Continuous positive airway pressure
NIV: Non-invasive ventilation
HFNC: High flow nasal canula

Figure 2: Invasive mechanical ventilation (met intubation criteria): Number of patients who met the clinical criteria for intubation (whether they were intubated or not).

Lower scores favour non-invasive ventilation.

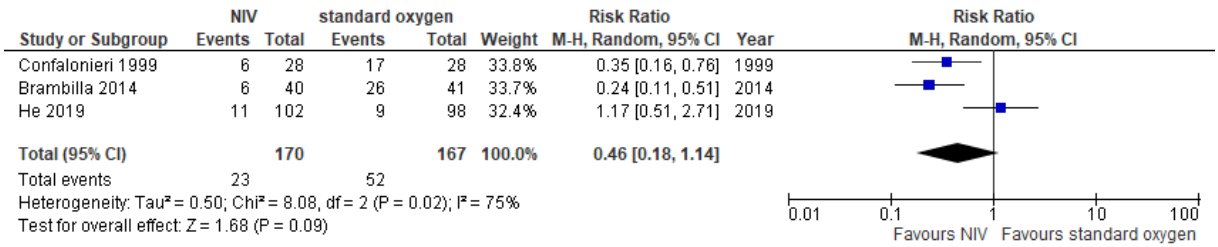
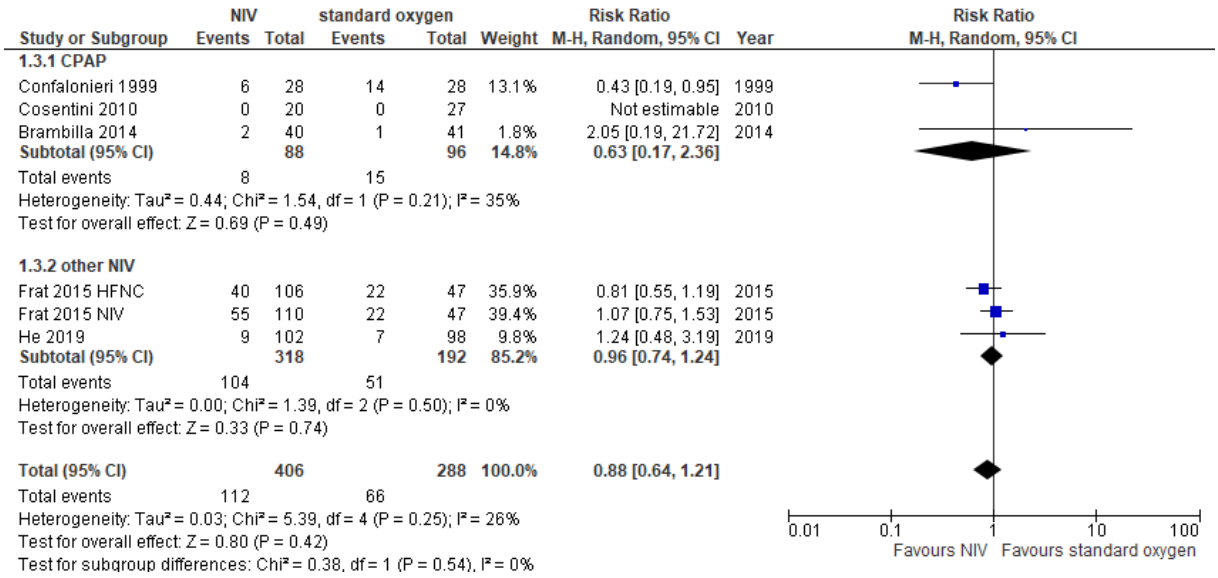


Figure 3: Invasive mechanical ventilation (intubation carried out): Number of patients who were intubated.

Lower scores favour non-invasive ventilation.



Abbreviations:
CPAP: Continuous positive airway pressure
NIV: Non-invasive ventilation
HFNC: High flow nasal canula

Figure 4: Duration of hospitalisation: Mean duration of hospital stay in days.

Lower scores favour non-invasive ventilation

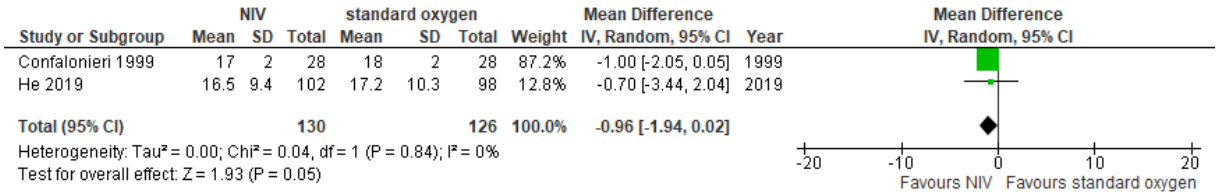


Figure 5: Duration of Intubation: Mean duration of intubation stay in days for patients who had been intubated.

Lower scores favour non-invasive ventilation

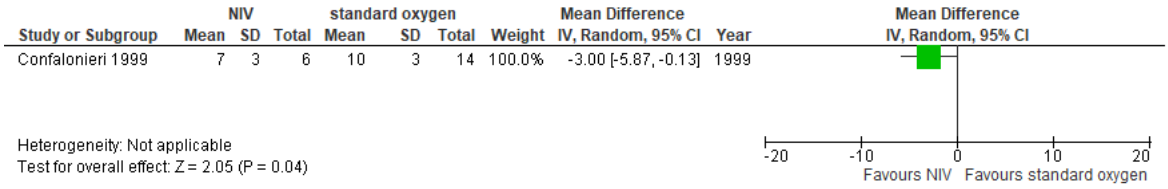
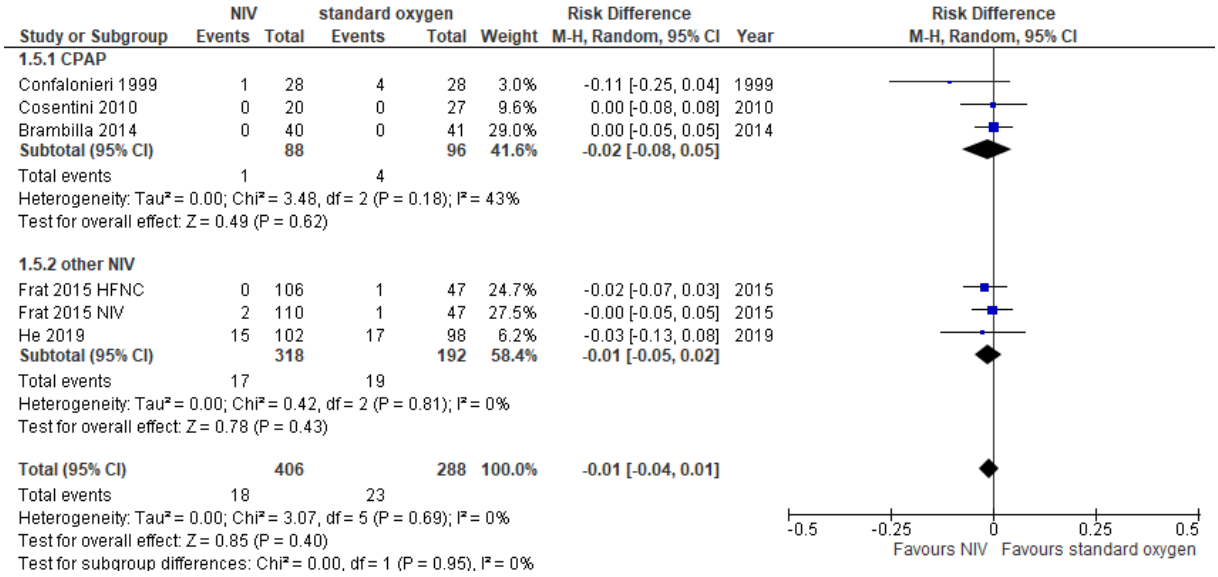


Figure 6: Adverse events: Number of patients who experienced adverse events at any follow up.

Lower scores favour non-invasive ventilation



Abbreviations:
CPAP: Continuous positive airway pressure
NIV: Non-invasive ventilation
HFNC: High flow nasal canula

1.4.4 Prospective cohort studies of continuous positive airway pressure vs NIV in adults

Figure 7: Mortality: Number of patients who had died at follow-up under 30 days.

Lower scores favour continuous positive airway pressure.

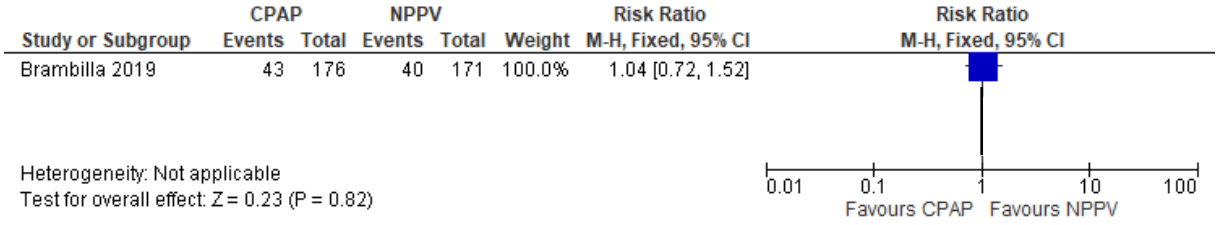
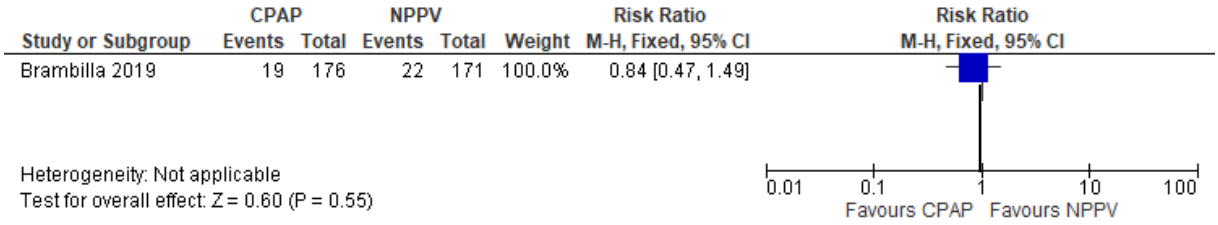


Figure 8: Invasive mechanical ventilation (intubation carried out): Number of patients who were intubated.

Lower scores favour continuous positive airway pressure



1.4.5 RCTs of high flow nasal oxygen vs CPAP in babies, children and young people

Figure 9: Invasive mechanical ventilation (intubation carried out): Number of patients who were intubated.

Lower scores favour high flow nasal canula.

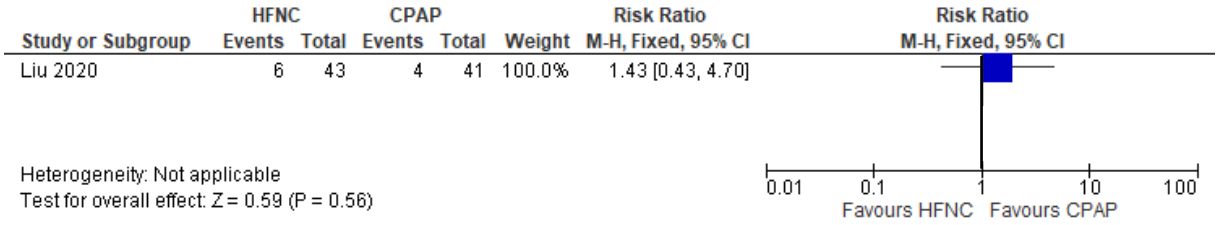


Figure 10: Duration of hospitalisation: Mean duration of hospital stay in days.

Lower scores favour high flow nasal canula

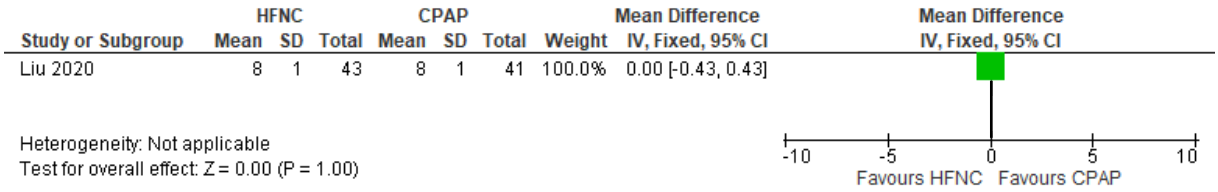


Figure 11: Duration of Intubation: Mean duration of intubation stay in days for patients who had been intubated.

Lower scores favour high flow nasal canula

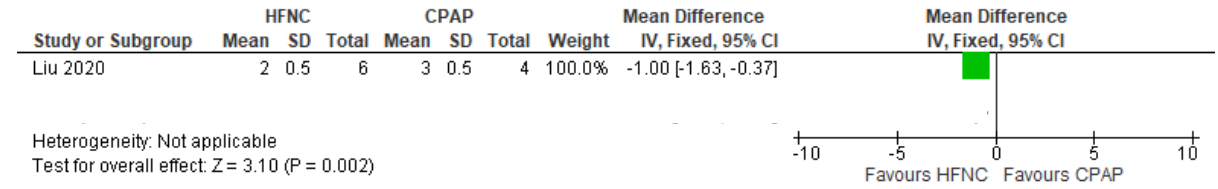


Figure 12: Adverse events: Number of patients who experienced adverse events at any follow up.

Lower scores favour high flow nasal canula

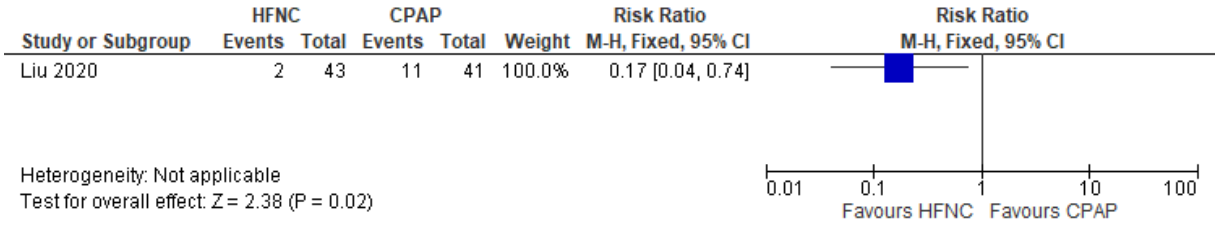
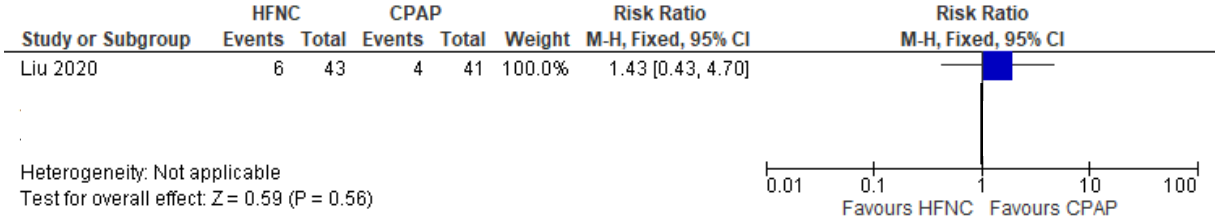


Figure 13: ICU admission: Number of patients who had been admitted to ICU (who were not in ICU at baseline)

Lower scores favour high flow nasal canula



1.4.6 RCTs of high flow nasal oxygen vs standard oxygen in babies, children and young people

Figure 14: Mortality: Number of patients who had died at follow-up under 30 days.

Lower scores favour high flow nasal canula

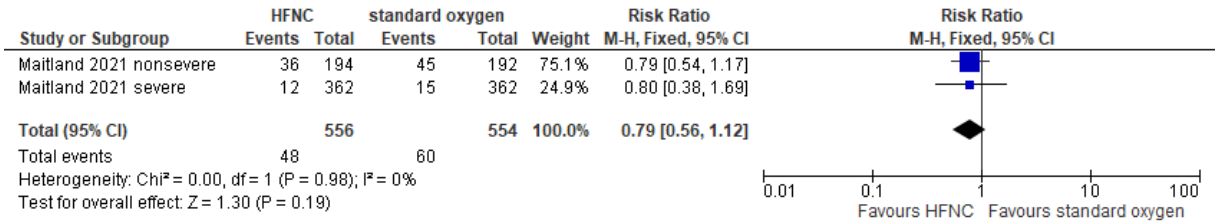


Figure 15: Duration of hospitalisation: Mean duration of hospital stay in days.

Lower scores favour high flow nasal canula

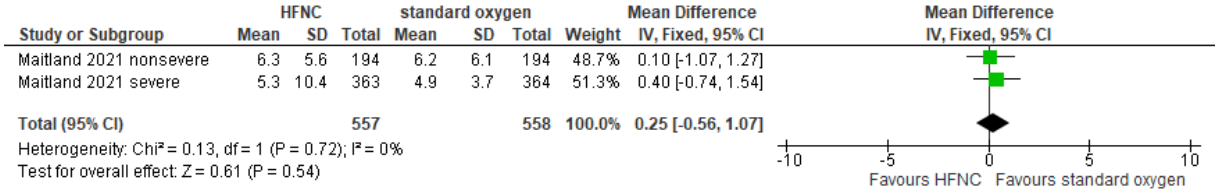


Figure 16: Adverse events: Number of patients who experienced adverse events at any follow up.

Lower scores favour high flow nasal canula

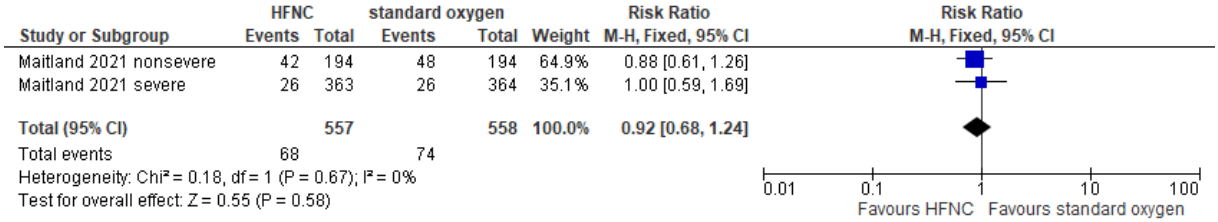
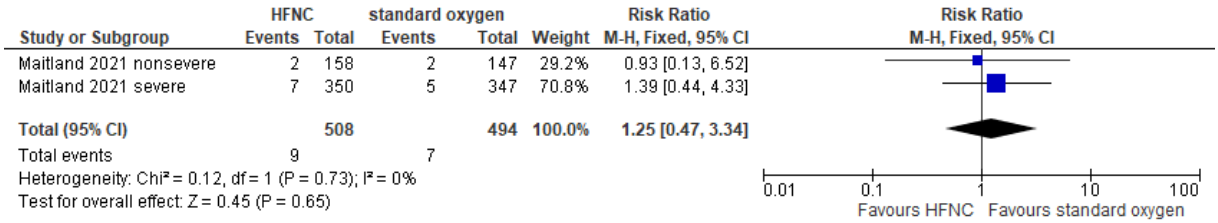


Figure 17: Hospital re-admission: Number of patients who had been re-admitted to hospital after discharge, within 28 days follow up.

Lower scores favour high flow nasal canula



Appendix F – GRADE tables

1.4.7 GRADE table for RCTs of non-invasive ventilation vs. standard oxygen in adults

Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	Standard oxygen	Relative (95% CI)	Absolute	
Mortality											
5[1,2,3,4,5]	randomised trials	no serious risk of bias	no serious inconsistency	serious[6]	very serious[7]	none	60/406 (14.8%)	42/288 (14.6%)	RR 0.83 (0.53 to 1.31)	25 fewer per 1000 (from 69 fewer to 45 more)	⊕OOO VERY LOW
Mortality – CPAP											
3[1,2,3]	randomised trials	no serious risk of bias	serious[8]	no serious indirectness	very serious[7]	none	9/88 (10.2%)	13/96 (13.5%)	RR 0.66 (0.17 to 2.57)	46 fewer per 1000 (from 112 fewer to 213 more)	⊕OOO VERY LOW
Mortality - other NIV											
2[4,5]	randomised trials	no serious risk of bias	serious[9]	serious[6]	very serious[7]	none	51/318 (16%)	29/192 (15.1%)	RR 0.86 (0.5 to 1.47)	21 fewer per 1000 (from 76 fewer to 71 more)	⊕OOO VERY LOW
Met intubation criteria											
3[1,2,4]	randomised trials	no serious risk of bias	very serious[10]	no serious indirectness	serious[11]	none	23/170 (13.5%)	52/167 (31.1%)	RR 0.46 (0.18 to 1.14)	168 fewer per 1000 (from 255 fewer to 44 more)	⊕OOO VERY LOW
Intubation carried out											
5[1,2,3,4,5]	randomised trials	no serious risk of bias	no serious inconsistency	very serious[12]	serious[11]	none	112/406 (27.6%)	66/288 (22.9%)	RR 0.88 (0.64 to 1.21)	28 fewer per 1000 (from 83 fewer to 48 more)	⊕OOO VERY LOW
Intubation carried out – CPAP											

3[1,2,3]	randomised trials	no serious risk of bias	serious[9]	no serious indirectness	very serious[7]	none	8/88 (9.1%)	15/96 (15.6%)	RR 0.63 (0.17 to 2.36)	58 fewer per 1000 (from 130 fewer to 212 more)	⊕OOO VERY LOW
Intubation carried out - other NIV											
2[4,5]	randomised trials	no serious risk of bias	no serious inconsistency	very serious[12]	serious[11]	none	104/318 (32.7%)	51/192 (26.6%)	RR 0.96 (0.74 to 1.24)	11 fewer per 1000 (from 69 fewer to 64 more)	⊕OOO VERY LOW
Duration of hospital stay (Better indicated by lower values) [MID:4.57]											
2[2,4]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	130	126	-	MD 0.96 lower (1.94 lower to 0.02 higher)	⊕⊕⊕⊕ HIGH
Adverse events											
5[1,2,3,4,5]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	18/406 (4.4%)	23/288 (8%)	RD -0.01 (-0.04 to 0.01)	22 fewer per 1000 (from 47 fewer to 25 more)	⊕⊕OO LOW
Adverse events – CPAP											
3[1,2,3]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	1/88 (1.1%)	4/96 (4.2%)	RD -0.02 (-0.08 to 0.05)	31 fewer per 1000 (from 40 fewer to 46 more)	⊕⊕OO LOW
Adverse events - other NIV											
2[4,5]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	None	17/318 (5.3%)	19/192 (9.9%)	RD -0.01 (-0.05 to 0.02)	20 fewer per 1000 (from 55 fewer to 46 more)	⊕⊕OO LOW
Duration of intubation (Better indicated by lower values) [MID: 1.5]											
1[2]	randomised trials	no serious risk of bias	Very serious[13]	no serious indirectness	no serious imprecision	none	6	14	-	MD 3 lower (5.87 to 0.13 lower)	⊕⊕OO LOW

1 Brambilla 2014

2 Confalonieri 1999

3 Cosentini 2010

4 He 2019

[5] Frat 2015

[6] Downgraded once as greater than 33.3% of the weight in the meta-analysis came from indirect or partially direct studies (Frat 2015)

[7] Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)

[8] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 58%)

[9] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 34%)

[10] Downgraded twice as the I2 was greater than 66.7% (I2 = 75%)

[11] Downgraded once as 95%CI crosses one clinical decision threshold (0.8)

[12] Downgraded twice as greater than 66.6% of the weight in the meta-analysis came from indirect or partially direct studies (Frat 2015)

[13] Downgraded twice due to small sample size from a single study

1.4.8 GRADE table for RCTs of non-invasive ventilation vs. standard oxygen in adults

Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CPAP	NPPV	Relative (95% CI)	Absolute	
Mortality											
1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	very serious [4]	none	43/176 (24.4%)	40/171 (23.4%)	RR 1.04 (0.72 to 1.52)	9 more per 1,000 (from 65 fewer to 122 more)	⊕OOO VERY LOW
Intubation carried out											

1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	very serious[4]	none	19/176 (10.8%)	22/171 (12.9%)	RR 0.84 (0.47 to 1.49)	21 fewer per 1,000 (from 68 fewer to 63 more)	⊕OOO VERY LOW

1 Brambilla 2019

2 Downgraded once for inconsistency: single study

3 Downgraded once for indirectness: single study rated as being indirectly applicable due to no control group

4 Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)

1.4.9 GRADE table RCTs of high flow nasal oxygen vs. CPAP in babies, children and young people

Quality assessment							No of patients		Effect		Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**HFNC**	**CPAP**	**Relative (95% CI)**	**Absolute**	
Mortality											
1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	no serious imprecision	none	0/43 (0%)	0/41 (0%)	RD 0.00 (-0.05 to 0.05)	0 more per 1000	⊕⊕OO LOW
Intubation carried out											
1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	very serious[4]	none	6/43 (14%)	4/41 (9.8%)	RR 1.43 (0.43 to 4.7)	42 more per 1000 (from 56	⊕OOO VERY LOW

										fewer to 361 more)	
Duration of hospital stay (Better indicated by lower values) [MID: 0.5]											
1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	serious	none	43	41	-	MD 0 higher (0.43 lower to 0.43 higher)	⊕OOO VERY LOW
Adverse events											
1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	no serious imprecision	none	2/43 (4.7%)	11/41 (26.8%)	RR 0.17 (0.04 to 0.74)	223 fewer per 1000 (from 70 fewer to 258 fewer)	⊕⊕OO LOW
Duration of intubation (Better indicated by lower values) [MID: 0.25]											
1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	no serious imprecision	none	6	4	-	MD 1 lower (1.63 to 0.37 lower)	⊕⊕OO LOW
ICU admission											
1[1]	randomised trials	no serious risk of bias	serious[2]	serious[3]	very serious[4]	none	6/43 (14%)	4/41 (9.8%)	RR 1.43 (0.43 to 4.7)	42 more per 1000 (from 56 fewer to 361 more)	⊕OOO VERY LOW

[1] Liu 2020

[2] Downgraded once for inconsistency: single study

[3] Downgraded once for indirectness: single study rated as being indirectly applicable due to no control group

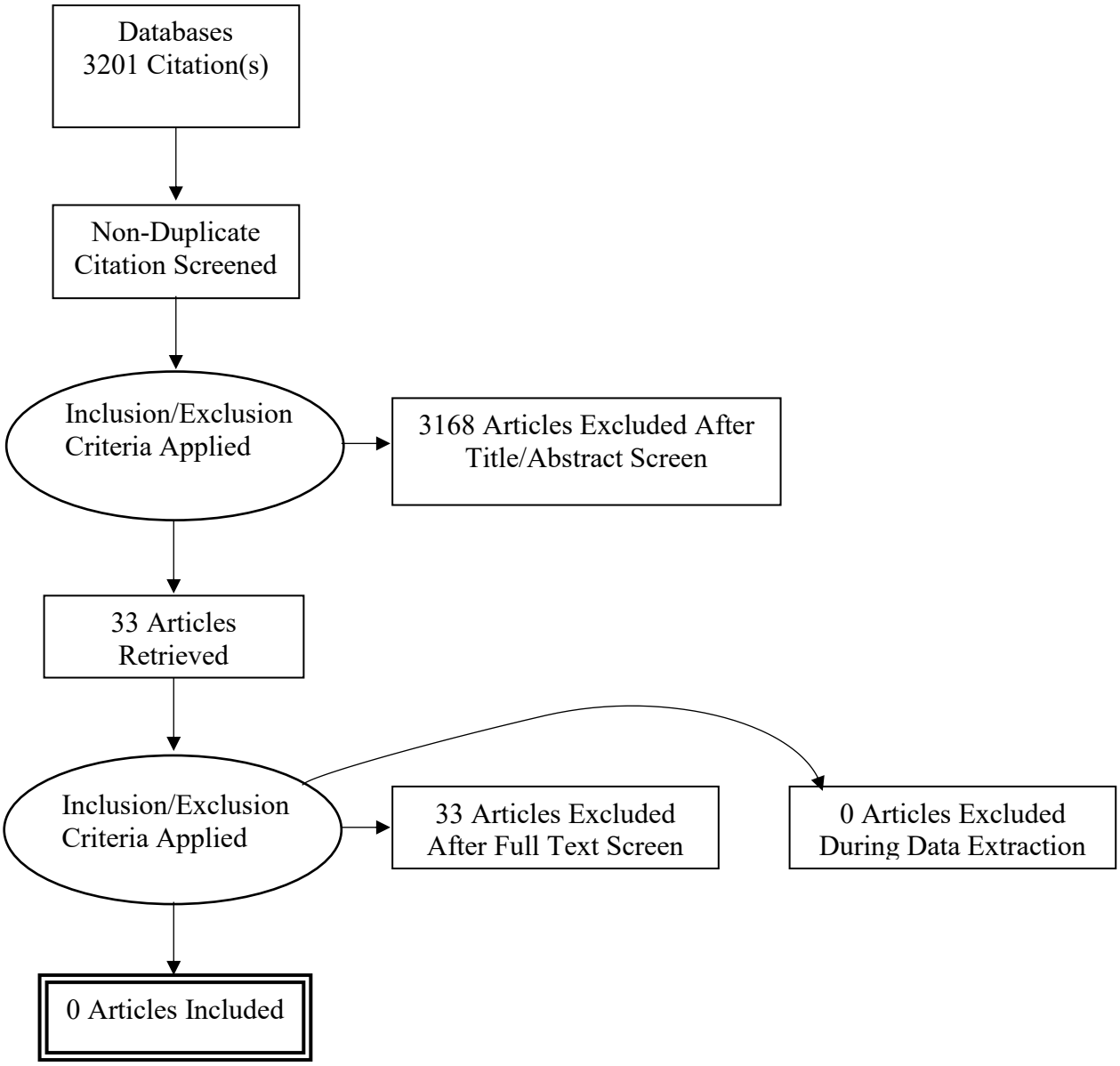
[4] Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)

1.4.10 GRADE table for RCTs of high flow nasal oxygen vs. standard oxygen in babies, children and young people

Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HFNC	Standard oxygen	Relative (95% CI)	Absolute	
Mortality											
1[1]	randomised trials	very serious[2]	serious[3]	very serious[4]	serious[5]	none	48/556 (8.6%)	60/554 (10.8%)	RR 0.79 (0.56 to 1.12)	23 fewer per 1000 (from 48 fewer to 13 more)	⊕OOO VERY LOW
Duration of hospitalisation (Better indicated by lower values) [MID: 2.36]											
1[1]	randomised trials	very serious[2]	serious[3]	very serious[4]	no serious imprecision	none	557	558	-	MD 0.25 higher (0.56 lower to 1.07 higher)	⊕OOO VERY LOW
Adverse events											
1[1]	randomised trials	very serious[2]	serious[3]	very serious[4]	serious[5]	none	68/557 (12.2%)	74/558 (13.3%)	RR 0.92 (0.68 to 1.24)	11 fewer per 1000 (from 42 fewer to 32 more)	⊕OOO VERY LOW
Hospital readmission											
1[1]	randomised trials	very serious[2]	serious[3]	very serious[4]	very serious[6]	none	9/508 (1.8%)	7/494 (1.4%)	RR 1.25 (0.47 to 3.34)	4 more per 1000 (from 8 fewer to 33 more)	⊕OOO VERY LOW

[1] Maitland 2021
[2] Downgraded twice for risk of bias: single study at high risk of bias
[3] Downgraded once for inconsistency: single study
[4] Downgraded once for indirectness: single study only partially applicable
[5] Downgraded once as 95%CI crosses one clinical decision threshold (0.8)
[6] Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

No studies were included in this review question.

Appendix I – Health economic model

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

Appendix J – Excluded studies

RCT Non-invasive ventilation in adults

Study	Code [Reason]
Ahmed, A.T., Abou Galalah, A.A., Mahgoub, A.A. et al. (2021) Comparative study between non-invasive ventilation with continuous positive airway pressure mask versus stacked breathing on chest expansion and pulmonary function in patients with pneumonia. Anaesthesia, Pain and Intensive Care 25(2): 176-184	- Comparator in study does not match that specified in protocol *NIV is the comparator, and the intervention is not included in the protocol*
Artaud-Macari, Elise, Bubenheim, Michael, Le Bouar, Gurvan et al. (2021) High-flow oxygen therapy versus non-invasive ventilation: a randomised physiological crossover study of alveolar recruitment in acute respiratory failure. ERJ open research 7(4)	- Data not reported in an extractable format *Crossover study, with only limited data available after first treatment. No relevant outcomes.*
Beng Leong, Lim; Wei Ming, Ng; Wei Feng, Lee (2019) High flow nasal cannula oxygen versus non-invasive ventilation in adult acute respiratory failure: a systematic review of randomized-controlled trials. European journal of emergency medicine : official journal of the European Society for Emergency Medicine 26(1): 9-18	- Systematic review used as source of primary studies *No eligible studies identified*
Cutuli, Salvatore Lucio, Grieco, Domenico Luca, Menga, Luca Salvatore et al. (2021) Non-invasive ventilation and high-flow oxygen therapy for severe community-acquired pneumonia. Current opinion in infectious diseases 34(2): 142-150	- Review article but not a systematic review
David-Joao, Paula G, Guedes, Murilo H, Rea-Neto, Alvaro et al. (2019) Non-invasive ventilation in acute hypoxemic respiratory failure: A systematic review and meta-analysis. Journal of critical care 49: 84-91	- Conference abstract
Hao, Jingjing, Liu, Jingyuan, Pu, Lin et al. (2023) High-Flow Nasal Cannula Oxygen Therapy versus Non-Invasive Ventilation in AIDS Patients with Acute Respiratory Failure: A Randomized Controlled Trial. Journal of clinical medicine 12(4)	- *Excluded participant group: Immunocompromised (HIV)*
Klefti, Giovana and Hill, Adam T (2020) The benefits of non-invasive ventilation for Community-Acquired Pneumonia: A meta-analysis. QJM : monthly journal of the Association of Physicians	- Systematic review used as source of primary studies *No eligible studies: all outside of date range*
Leung, C C H, Joynt, G M, Gomersall, C D et al. (2019) Comparison of high-flow nasal cannula versus oxygen face mask for environmental bacterial contamination in critically ill pneumonia patients: a randomized controlled crossover trial. The Journal of hospital infection 101(1): 84-87	- Does not contain relevant outcomes

Study	Code [Reason]
Liesching, T.N. and Lei, Y. (2019) Efficacy of High-Flow Nasal Cannula Therapy in Intensive Care Units: A Meta-Analysis of Physiological and Clinical Outcomes. Journal of Intensive Care Medicine 34(2): 140-152	- Review article checked for references
Peters, Steve G; Holets, Steven R; Gay, Peter C (2013) High-flow nasal cannula therapy in do-not-intubate patients with hypoxemic respiratory distress. Respiratory care 58(4): 597-600	- Not a relevant study design *Retrospective patient review*
Ruzsics, Istvan, Matrai, Peter, Hegyi, Peter et al. (2022) Non-invasive ventilation improves the outcome in patients with pneumonia-associated respiratory failure: Systematic review and meta-analysis. Journal of infection and public health 15(3): 349-359	- Systematic review used as source of primary studies *No eligible studies: all outside of date range*
Vanoni, Nicolo Maria, Carugati, Manuela, Borsa, Noemi et al. (2019) Management of Acute Respiratory Failure Due to Community-Acquired Pneumonia: A Systematic Review. Medical sciences (Basel, Switzerland) 7(1)	- Review article checked for references
Wijesinghe, M, Perrin, K, Weatherall, M et al. (2009) A randomised controlled trial of high flow versus titrated oxygen therapy in the management of patients with community acquired pneumonia. Respirology (Carlton, Vic.) 14(suppl1): a83	- Conference abstract
Xing, Dong, Chen, Li, Wang, Lantao et al. (2022) An analysis of the treatment effect of two modes of oxygenation on patients with radiation pneumonia complicated by respiratory failure. Technology and health care : official journal of the European Society for Engineering and Medicine 30(4): 869-880	- *Radiation pneumonia is excluded*

Abbreviations:
CPAP: Continuous positive airway pressure
NIV: Non-invasive ventilation
HFNC: High flow nasal canula

RCT Non-invasive ventilation in babies, children and young people

Study	Code [Reason]
Brambilla, Anna Maria, Aliberti, Stefano, Prina, Elena et al. (2014) Helmet CPAP vs. oxygen therapy in severe hypoxemic respiratory failure due to pneumonia. Intensive care medicine 40(7): 942-9	- *Adult population*
Chaves, Gabriela Ss, Freitas, Diana A, Santino, Thayla A et al. (2019) Chest physiotherapy for pneumonia in children. The Cochrane database of systematic reviews 1: cd010277	- SR checked for references

Study	Code [Reason]
Chisti, Mohammod J, Salam, Mohammed A, Smith, Jonathan H et al. (2015) Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. Lancet (London, England) 386(9998): 1057-65	- Study does not contain a relevant intervention *Bubble CPAP not used in the UK*
Cosentini, R Brambilla, AM Aliberti, S Bignamini, A Nava, S Maffei, A Martinotti, R Tarsia, P Monzani, V Pelosi, P (2010) Helmet Continuous Positive Airway Pressure vs Oxygen Therapy To Improve Oxygenation in Community-Acquired Pneumonia A Randomized, Controlled Trial. CHEST 138(1): 114 - 120	- Population are adults
Falsaperla, Raffaele, Elli, Marco, Pavone, Piero et al. (2013) Non-invasive ventilation for acute respiratory distress in children with central nervous system disorders. Respiratory medicine 107(9): 1370-5	- Population is *Immunocompromised*
Gebre, Meseret, Haile, Kassa, Duke, Trevor et al. (2022) Effectiveness of Bubble Continuous Positive Airway Pressure (BCPAP) for Treatment of Children Aged 1-59 Months with Severe Pneumonia and Hypoxemia in Ethiopia: A Pragmatic Cluster Randomized Controlled Clinical Trial. Journal of clinical medicine 11(17)	- Study does not contain a relevant intervention *Bubble CPAP not used in the UK*
Jayashree, Muralidharan, KiranBabu, H B, Singhi, Sunit et al. (2016) Use of Nasal Bubble CPAP in Children with Hypoxemic Clinical Pneumonia-Report from a Resource Limited Set-Up. Journal of tropical pediatrics 62(1): 69-74	- Study does not contain a relevant intervention *Bubble CPAP not used in the UK*
Maitland, Kathryn, Kiguli, Sarah, Opoka, Robert O et al. (2017) Children's Oxygen Administration Strategies Trial (COAST): A randomised controlled trial of high flow versus oxygen versus control in African children with severe pneumonia. Wellcome open research 2: 100	- Secondary publication of an included study that does not provide any additional relevant information
McCollum, Eric D, Mvalo, Tisungane, Eckerle, Michelle et al. (2019) Bubble continuous positive airway pressure for children with high-risk conditions and severe pneumonia in Malawi: an open label, randomised, controlled trial. The Lancet. Respiratory medicine 7(11): 964-974	- Population are i*mmunocompromised (mostly HIV+)*
Modesto I Alapont, Vicent, Khemani, Robinder G, Medina, Alberto et al. (2017) Bayes to the Rescue: Continuous Positive Airway Pressure Has Less Mortality Than High-Flow Oxygen. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies 18(2): e92-e99	- Secondary publication of an excluded study - *Bayesian analysis of Chisti 2015*

Study	Code [Reason]
Sessions, Kristen L, Mvalo, Tisungane, Kondowe, Davie et al. (2019) Bubble CPAP and oxygen for child pneumonia care in Malawi: a CPAP IMPACT time motion study. BMC health services research 19(1): 533	- Population are *Immunocompromised (HIV+)*
Wilkes, Chris, Subhi, Rami, Graham, Hamish R et al. (2022) Continuous Positive Airway Pressure (CPAP) for severe pneumonia in low- and middle-income countries: A systematic review of contextual factors. Journal of global health 12: 10012	- SR checked for references
Yapicioglu, Hacer, Yildizdas, Dincer, Bayram, Ibrahim et al. (2003) The use of surfactant in children with acute respiratory distress syndrome: efficacy in terms of oxygenation, ventilation and mortality. Pulmonary pharmacology & therapeutics 16(6): 327-33	- Not a relevant intervention – invasive ventilation
Zhao, Xueqin; Qin, Qiaozhi; Zhang, Xian (2021) Outcomes of High-Flow Nasal Cannula Vs. Nasal Continuous Positive Airway Pressure in Young Children With Respiratory Distress: A Systematic Review and Meta-Analysis. Frontiers in pediatrics 9: 759297	- SR checked for references

Abbreviations:
CPAP: Continuous positive airway pressure
NIV: Non-invasive ventilation
HFNC: High flow nasal canula

Prospective cohorts Non-invasive ventilation in adults, babies, children and young people

Study	Code [Reason]
Al-Rajhi, Amjad, Murad, Anwar, Li, P Z et al. (2018) Outcomes and predictors of failure of non-invasive ventilation in patients with community acquired pneumonia in the ED. The American journal of emergency medicine 36(3): 347-351	- Not a relevant study design: Retrospective
Antonelli, M, Conti, G, Moro, M L et al. (2001) Predictors of failure of non-invasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. Intensive care medicine 27(11): 1718-28	- Population contains <75% pneumonia patients
Antonucci, E., Giovini, M., Cecchia, M. et al. (2023) High-Flow Nasal Oxygen versus Continuous Positive Airway Pressure in patients with hypoxemic acute respiratory failure due to pneumonia. Trends in Anaesthesia and Critical Care 50: 101248	- Not a relevant study design: Retrospective
Azevedo, Luciano C P, Park, Marcelo, Salluh, Jorge I F et al. (2013) Clinical outcomes of patients requiring ventilatory support in Brazilian intensive care units: a multicenter,	- Population contains <75% pneumonia patients

Study	Code [Reason]
prospective, cohort study. Critical care (London, England) 17(2): r63	
Besen, Bruno A M P; Park, Marcelo; Ranzani, Otavio T (2021) Non-invasive ventilation in critically ill very old patients with pneumonia: A multicenter retrospective cohort study. PloS one 16(1): e0246072	- Not a relevant study design: Retrospective
Bustos-Gajardo, F D, Luarte-Martinez, S I, Dubo Araya, S A et al. (2023) Clinical outcomes according to timing to invasive ventilation due to non-invasive ventilation failure in children. Medicina intensiva 47(2): 65-72	- No comparison between treatments
Carrillo, Andres, Gonzalez-Diaz, Gumersindo, Ferrer, Miquel et al. (2012) Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. Intensive care medicine 38(3): 458-66	- No comparison between treatments
Carron, Michele, Freo, Ulderico, Zorzi, Manuel et al. (2010) Predictors of failure of non-invasive ventilation in patients with severe community-acquired pneumonia. Journal of critical care 25(3): 540e9-14	- No comparison between treatments
Carteaux, Guillaume, Millan-Guilarte, Teresa, De Prost, Nicolas et al. (2016) Failure of Non-invasive Ventilation for De Novo Acute Hypoxemic Respiratory Failure: Role of Tidal Volume. Critical care medicine 44(2): 282-90	- No comparison between treatments
Chang, Chih-Ching, Lin, Yi-Chen, Chen, Tzu-Chun et al. (2021) High-Flow Nasal Cannula Therapy in Children With Acute Respiratory Distress With Hypoxia in A Pediatric Intensive Care UnitA Single Center Experience. Frontiers in pediatrics 9: 664180	- Not a relevant study design: Retrospective
Chen, Lu-Lu, Weng, Heng, Li, Hong-Yan et al. (2023) Non-invasive Mechanical Ventilation in Patients with Viral Pneumonia-Associated Acute Respiratory Distress Syndrome: An Observational Retrospective Study. International journal of clinical practice 2023: 1819087	- Not a relevant study design: Retrospective
Esquinas Rodriguez, Antonio M, Papadakos, Peter J, Carron, Michele et al. (2013) Clinical review: Helmet and non-invasive mechanical ventilation in critically ill patients. Critical care (London, England) 17(2): 223	- Systematic review. Checked for possible includes
Fortenberry, J D, Del Toro, J, Jefferson, L S et al. (1995) Management of pediatric acute hypoxemic respiratory insufficiency with bilevel positive pressure (BiPAP) nasal mask ventilation. Chest 108(4): 1059-64	- Not a relevant study design: Retrospective
Ilieva, Viktoria and Yamakova, Yordanka (2021) Non-invasive ventilation: a safe and effective respiratory support method in hypoxemic acute respiratory failure due to pneumonia with or without acute respiratory distress syndrome. Folia medica 63(3): 321-328	- No comparison between treatments

Study	Code [Reason]
Ito, Jiro, Nagata, Kazuma, Morimoto, Takeshi et al. (2019) Respiratory management of acute exacerbation of interstitial pneumonia using high-flow nasal cannula oxygen therapy: a single center cohort study. Journal of thoracic disease 11(1): 103-112	- Not a relevant study design: Retrospective
Jolliet, P, Abajo, B, Pasquina, P et al. (2001) Non-invasive pressure support ventilation in severe community-acquired pneumonia. Intensive care medicine 27(5): 812-21	- Population contains <75% pneumonia patients *Mixed population with HIV and cancer*
Koga, Yasutaka, Kaneda, Kotaro, Fujii, Nao et al. (2020) Comparison of high-flow nasal cannula oxygen therapy and non-invasive ventilation as first-line therapy in respiratory failure: a multicenter retrospective study. Acute medicine & surgery 7(1): e461	- Not a relevant study design: Retrospective
L'HerE, Moriconi, M, Texier, F et al. (1998) Non-invasive continuous positive airway pressure in acute hypoxaemic respiratory failure--experience of an emergency department. European journal of emergency medicine : official journal of the European Society for Emergency Medicine 5(3): 313-8	- Not a relevant study design: Retrospective
Lenglet, Hugo, Sztrymf, Benjamin, Leroy, Christophe et al. (2012) Humidified high flow nasal oxygen during respiratory failure in the emergency department: feasibility and efficacy. Respiratory care 57(11): 1873-8	- Population contains <75% pneumonia patients
Liesching, T.N. and Lei, Y. (2019) Efficacy of High-Flow Nasal Cannula Therapy in Intensive Care Units: A Meta-Analysis of Physiological and Clinical Outcomes. Journal of Intensive Care Medicine 34(2): 140-152	- Systematic review. Checked for possible includes
Mandelzweig, K., Leligdowicz, A., Murthy, S. et al. (2018) Non-invasive ventilation in children and adults in low- and low-middle income countries: A systematic review and meta-analysis. Journal of Critical Care 47: 310-319	- Systematic review. Checked for possible includes
Messika, Jonathan, Ben Ahmed, Karim, Gaudry, Stephane et al. (2015) Use of High-Flow Nasal Cannula Oxygen Therapy in Subjects With ARDS: A 1-Year Observational Study. Respiratory care 60(2): 162-9	- No comparison between treatments *relevant outcomes only reported for HFNC*
Miller, David C, Pu, Jie, Kukafka, David et al. (2022) Failure of High Flow Nasal Cannula and Subsequent Intubation Is Associated With Increased Mortality as Compared to Failure of Non-Invasive Ventilation and Mechanical Ventilation Alone: A Real-World Retrospective Analysis. Journal of intensive care medicine 37(1): 41-45	- Not a relevant study design: Retrospective
Modesto I Alapont, V., Khemani, R.G., Medina, A. et al. (2017) Bayes to the Rescue: Continuous Positive Airway Pressure Has Less Mortality Than High-Flow Oxygen. Pediatric Critical Care Medicine 18(2): e92-e99	- Bubble CPAP method not used in UK

Study	Code [Reason]
Murad, A, Li, P Z, Dial, S et al. (2015) The role of non-invasive positive pressure ventilation in community-acquired pneumonia. Journal of critical care 30(1): 49-54	- Not a relevant study design: Retrospective
Nicolini, Antonello, Ferraioli, Gianluca, Ferrari-Bravo, Maura et al. (2016) Early non-invasive ventilation treatment for respiratory failure due to severe community-acquired pneumonia. The clinical respiratory journal 10(1): 98-103	- No comparison between treatments
Nicolini, Antonello, Piroddi, Ines Maria Grazia, Barlascini, Cornelius et al. (2014) Predictors of non-invasive ventilation failure in severe respiratory failure due to community acquired pneumonia. Tanaffos 13(4): 20-8	- Not a relevant study design: Retrospective
Norkiene, Ieva; d'Espiney, Raquel; Martin-Lazaro, Juan F (2019) Effectiveness of high-flow nasal oxygen therapy in management of acute hypoxemic and hypercapnic respiratory failure. Acta medica Lituanica 26(1): 46-50	- Not a relevant study design: Retrospective
Omote, Norihito, Matsuda, Naoyuki, Hashimoto, Naozumi et al. (2020) High-flow nasal cannula therapy for acute respiratory failure in patients with interstitial pneumonia: a retrospective observational study. Nagoya journal of medical science 82(2): 301-313	- Not a relevant study design: Retrospective
Ortin, A., Jimenez, R., Rebollo, S. et al. (2015) Outcome of patients with initial non-mechanical ventilation management in severe pneumonia. Intensive Care Medicine Experimental 3(supplement1): a95	- Conference abstract
Paolini, Valentina, Faverio, Paola, Aliberti, Stefano et al. (2018) Positive end expiratory pressure in acute hypoxemic respiratory failure due to community acquired pneumonia: do we need a personalized approach?. PeerJ 6: e4211	- No comparison between treatments *Comparison was within subjects, in a set order of escalating treatment.*
Park, Min Jeong, Cho, Jae Hwa, Chang, Youjin et al. (2020) Factors for Predicting Non-invasive Ventilation Failure in Elderly Patients with Respiratory Failure. Journal of clinical medicine 9(7)	- No comparison between treatments
Perazzo, A., Gatto, P., Colamartino, S. et al. (2015) Non-invasive ventilation in the treatment of severe community-acquired pneumonia: The experience of a single center. Infectious Diseases in Clinical Practice 23(4): 194-197	- No comparison between treatments
Polti, S., Meregalli, G., Messinesi, G. et al. (2006) Helmet CPAP in community acquired pneumonia with acute respiratory failure. Rassegna di Patologia dell'Apparato Respiratorio 21(1): 9-13	- Full text paper not available
Pons-Odena, Marti, Palanca, Daniel, Modesto, Vicent et al. (2013) SpO2/FiO2 as a predictor of non-invasive ventilation failure in children with hypoxemic respiratory insufficiency. Journal of pediatric intensive care 2(3): 111-119	- Not a relevant study design: Retrospective

Study	Code [Reason]
Rialp, Gemma, Forteza, Catalina, Muniz, Daniel et al. (2017) Role of First-Line Non-invasive Ventilation in Non-COPD Subjects With Pneumonia. Archivos de bronconeumologia 53(9): 480-488	- Study not reported in English
Roca, Oriol, Caralt, Berta, Messika, Jonathan et al. (2019) An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy. American journal of respiratory and critical care medicine 199(11): 1368-1376	- No comparison between treatments
Roca, Oriol, Messika, Jonathan, Caralt, Berta et al. (2016) Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: The utility of the ROX index. Journal of critical care 35: 200-5	- No comparison between treatments
Saelim, Kantara, Thirapaleka, Busawan, Ruangnapa, Kanokpan et al. (2022) Predictors of high-flow nasal cannula failure in pediatric patients with acute respiratory distress. Clinical and experimental pediatrics 65(12): 595-601	- Population contains <75% pneumonia patients
Smith, M.E.; Gray, M.; Wilson, P.T. (2023) Acceptance and Tolerability of Helmet CPAP in Pediatric Bronchiolitis and Pneumonia: A Feasibility Study. Journal of Pediatric Intensive Care	- Not a relevant study design: Retrospective
Song, Yamei, Zhang, Jinchao, Xing, Jia et al. (2021) Comparison of high-flow nasal oxygen cannula therapy versus a standard oxygen face mask in patients with hypostatic pneumonia. The Journal of international medical research 49(6): 3000605211022279	- Not a relevant study design: Retrospective
Stefan, Mihaela S, Priya, Aruna, Pekow, Penelope S et al. (2018) The comparative effectiveness of non-invasive and invasive ventilation in patients with pneumonia. Journal of critical care 43: 190-196	- Not a relevant study design: Retrospective
Sun, W., Luo, Z., Cao, Z. et al. (2022) A combination of the APACHE II score, neutrophil/lymphocyte ratio, and expired tidal volume could predict non-invasive ventilation failure in pneumonia-induced mild to moderate acute respiratory distress syndrome patients. Annals of Translational Medicine 10(7): 407	- Not a relevant study design: Retrospective
Sztrymf, Benjamin, Messika, Jonathan, Mayot, Thomas et al. (2012) Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. Journal of critical care 27(3): 324e9-13	- Population contains <75% pneumonia patients
Taha, Ahmed, Larumbe-Zabala, Eneko, Abugroun, Ashraf et al. (2019) Outcomes of Non-invasive Positive Pressure Ventilation in Acute Respiratory Distress Syndrome and Their Predictors: A National Cohort. Critical care research and practice 2019: 8106145	- Not a relevant study design: Retrospective

Study	Code [Reason]
Tomii, Keisuke, Tachikawa, Ryo, Chin, Kazuo et al. (2010) Role of non-invasive ventilation in managing life-threatening acute exacerbation of interstitial pneumonia. Internal medicine (Tokyo, Japan) 49(14): 1341-7	- Not a relevant study design: Retrospective
Valley, Thomas S, Walkey, Allan J, Lindenauer, Peter K et al. (2017) Association Between Non-invasive Ventilation and Mortality Among Older Patients With Pneumonia. Critical care medicine 45(3): e246-e254	- Not a relevant study design: Retrospective
Watson, Adam, Yadollahi, Sina, Fahmy, Alexander et al. (2023) Non-Invasive Ventilation for Community-Acquired Pneumonia: Outcomes and Predictors of Failure from an ICU Cohort. Medicina (Kaunas, Lithuania) 60(1)	- Not a relevant study design: Retrospective
Weir, Timothy E and Bihari, Shailesh (2024) Factors associated with intubation in patients with acute hypoxaemic respiratory failure treated with high-flow nasal cannula oxygen therapy: A prospective, observational study. Australian critical care : official journal of the Confederation of Australian Critical Care Nurses 37(3): 455-460	- No comparison between treatments
Wolfler, Andrea, Calderini, Edoardo, Iannella, Elisa et al. (2015) Evolution of Non-invasive Mechanical Ventilation Use: A Cohort Study Among Italian PICUs. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies 16(5): 418-27	- Not a relevant study design: Retrospective
Yokoyama, Toshiki, Tsushima, Kenji, Yamamoto, Hiroshi et al. (2012) Potential benefits of early continuous positive pressure ventilation in patients with rapidly progressive interstitial pneumonia. Respirology (Carlton, Vic.) 17(2): 315-21	- No comparison between treatments
Yurtseven, A. and Saz, E.U. (2020) The effectiveness of heated humidified high-flow nasal cannula in children with severe bacterial pneumonia in the emergency department. Journal of Pediatric Research 7(1): 71-76	- No comparison between treatments
Zhao, W-P, Zhang, W, Li, J-P et al. (2024) Factors influencing the therapeutic failure of high-flow nasal cannula oxygen humidification in patients with interstitial pneumonia complicated by respiratory failure. European review for medical and pharmacological sciences 28(7): 2770-2776	- Not a relevant study design: Retrospective
Zheng, Liling, Dai, Xiaojuan, Zheng, Weida et al. (2023) Comparative Analysis of High-Flow Nasal Cannula Oxygen Therapy and Invasive Mechanical Ventilation in the Management of Severe Pneumonia: A Retrospective Study. Alternative therapies in health and medicine	- Not a relevant study design: Retrospective

Abbreviations:
CPAP: Continuous positive airway pressure
NIV: Non-invasive ventilation
HFNC: High flow nasal canula

Economic

Study	Code [Reason]
Akyil, Fatma Tokgoz, Hazar, Armagan, Erdem, Ipek et al. (2015) Hospital Treatment Costs and Factors Affecting These Costs in Community-Acquired Pneumonia. Turkish thoracic journal 16(3): 107-113	- Study does not contain a relevant intervention *Costing study, does not compare interventions*
Andrews, Annie Lintzenich, Simpson, Annie N, Heine, Daniel et al. (2015) A Cost-Effectiveness Analysis of Obtaining Blood Cultures in Children Hospitalized for Community-Acquired Pneumonia. The Journal of pediatrics 167(6): 1280-6	- US study
Antunes, C, Pereira, M, Rodrigues, L et al. (2020) Hospitalization direct cost of adults with community-acquired pneumonia in Portugal from 2000 to 2009. Pulmonology 26(5): 264-267	- Study does not contain a relevant intervention *Costing study, does not compare interventions*
Asti, L, Bartsch, S M, Umscheid, C A et al. (2019) The potential economic value of sputum culture use in patients with community-acquired pneumonia and healthcare-associated pneumonia. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 25(8): 1038e1-1038e9	- US study
Buendia, Jefferson A and Patino, Diana Guerrero (2023) Corticosteroids for the treatment of respiratory infection by Mycoplasma pneumoniae in children: A cost-utility analysis. Pediatric pulmonology 58(10): 2809-2814	- Non OECD country *Columbia*
Cammarota, Gianmaria; Vetrugno, Luigi; Longhini, Federico (2023) Lung ultrasound monitoring: impact on economics and outcomes. Current opinion in anaesthesiology 36(2): 234-239	- Does not contain a population of people with only pneumonia, includes people with acute respiratory failure *Unclear if the patients are intubated* - US study *Unclear if the study is US or Europe* -Abstract only
Ceyhan, Mehmet, Ozsurekci, Yasemin, Aykac, Kubra et al. (2018) Economic burden of pneumococcal infections in children under 5 years of age. Human vaccines & immunotherapeutics 14(1): 106-110	- Study does not contain a relevant intervention *Non-comparative costing analysis*

Study	Code [Reason]
Cisco, Giulio, Meier, Armando N, Senn, Nicolas et al. (2024) Cost-effectiveness analysis of procalcitonin and lung ultrasonography guided antibiotic prescriptions in primary care. The European journal of health economics : HEPAC : health economics in prevention and care	- setting in primary care whereas the review was in secondary care
Costa, Nadege, Hoogendijk, Emiel O, Mounie, Michael et al. (2017) Additional Cost Because of Pneumonia in Nursing Home Residents: Results From the Incidence of Pneumonia and Related Consequences in Nursing Home Resident Study. Journal of the American Medical Directors Association 18(5): 453e7-453e12	- Study does not contain a relevant intervention *Non-comparative costing analysis*
Hyams, Catherine; Williams, O Martin; Williams, Philip (2020) Urinary antigen testing for pneumococcal pneumonia: is there evidence to make its use uncommon in clinical practice?. ERJ open research 6(1)	- Review article but not a systematic review, all primary studies were check for relevance
Ito, Akihiro, Ishida, Tadashi, Tokumasu, Hironobu et al. (2017) Impact of procalcitonin-guided therapy for hospitalized community-acquired pneumonia on reducing antibiotic consumption and costs in Japan. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy 23(3): 142-147	- Not a relevant study design *Costing study not a cost utility study*
Javanbakht, Mehdi, Moradi-Lakeh, Maziar, Mashayekhi, Atefeh et al. (2022) Continuous Monitoring of Respiratory Rate with Wearable Sensor in Patients Admitted to Hospital with Pneumonia Compared with Intermittent Nurse-Led Monitoring in the United Kingdom: A Cost-Utility Analysis. PharmacoEconomics - open 6(1): 73-83	- Study does not contain a relevant intervention *Continuous monitoring versus intermittent monitoring, NEWS used in both arms*
Khole, Aalok V, Dionne, Emily, Zitek-Morrison, Emily et al. (2023) Cefepime extended infusion versus intermittent infusion: Clinical and cost evaluation. Antimicrobial stewardship & healthcare epidemiology : ASHE 3(1): e119	- US study
Latif, Marina, Guo, Ning, Tereshchenko, Larisa G et al. (2023) Association of hospital spending with care patterns and mortality in patients hospitalized with community-acquired pneumonia. Journal of hospital medicine 18(11): 986-993	- Study does not contain a relevant intervention *US costing study with no comparative interventions*
Leem, Ah Young, Jung, Won Jai, Kang, Young Ae et al. (2014) Comparison of methicillin-resistant Staphylococcus aureus community-acquired and healthcare-associated pneumonia. Yonsei medical journal 55(4): 967-74	- Not a relevant study design *Not a health economic study*
Macaya, M.C.; Ridulfo, A.H.; Ramirez-Santana, M. (2015) Comparison of costs and health outcomes of users with community-acquired pneumonia treated at home or in traditional hospitalization: An exploratory study of 40 cases. Value in Health Regional Issues 8: 112-115	- Study not reported in English *Reported in Spanish*

Study	Code [Reason]
McKinnell, James A, Corman, Shelby, Patel, Dipen et al. (2018) Effective Antimicrobial Stewardship Strategies for Cost-effective Utilization of Telavancin for the Treatment of Patients With Hospital-acquired Bacterial Pneumonia Caused by Staphylococcus aureus. Clinical therapeutics 40(3): 406-414e2	- Study does not contain a relevant intervention *US study that compares different antibiotics rather than length of treatments*
Meacock, Rachel, Sutton, Matt, Kristensen, Soren Rud et al. (2017) Using Survival Analysis to Improve Estimates of Life Year Gains in Policy Evaluations. Medical decision making : an international journal of the Society for Medical Decision Making 37(4): 415-426	- Study does not contain a relevant intervention *Modelling survival not cost effectiveness of treatment*
Miners, Lisa, Huntington, Susie, Lee, Nathaniel et al. (2023) An economic evaluation of two PCR-based respiratory panel assays for patients admitted to hospital with community-acquired pneumonia (CAP) in the UK, France and Spain. BMC pulmonary medicine 23(1): 220	- Not a relevant study design *Cost consequence study*
Patel, Archana B, Bang, Akash, Singh, Meenu et al. (2015) A randomized controlled trial of hospital versus home based therapy with oral amoxicillin for severe pneumonia in children aged 3 - 59 months: The IndiaCLEN Severe Pneumonia Oral Therapy (ISPOT) Study. BMC pediatrics 15: 186	- Non OECD country *India*
Pliakos, Elina Eleftheria, Andreatos, Nikolaos, Tansarli, Giannoula S et al. (2019) The Cost-Effectiveness of Corticosteroids for the Treatment of Community-Acquired Pneumonia. Chest 155(4): 787-794	- US study
Prasath, T.M., Ramachandran, V., Geetha, S. et al. (2019) Hidden Markov model-based cough sound analysis for classification of asthma and pneumonia in pediatric. Drug Invention Today 11(7): 1692-1695	- Full text paper not available
Przybilla, Jens, Ahnert, Peter, Bogatsch, Holger et al. (2020) Markov State Modelling of Disease Courses and Mortality Risks of Patients with Community-Acquired Pneumonia. Journal of clinical medicine 9(2)	- Study does not contain a relevant intervention *Does not include costs*
Reynolds, Courtney A, Finkelstein, Jonathan A, Ray, G Thomas et al. (2014) Attributable healthcare utilization and cost of pneumonia due to drug-resistant streptococcus pneumonia: a cost analysis. Antimicrobial resistance and infection control 3: 16	- Study does not contain a relevant intervention *Looking at different antibiotics not the length of the courses*
Rozenbaum, Mark H, Mangen, Marie-Josee J, Huijts, Susanne M et al. (2015) Incidence, direct costs and duration of hospitalization of patients hospitalized with community acquired pneumonia: A nationwide retrospective claims database analysis. Vaccine 33(28): 3193-9	- Study does not contain a relevant intervention *Costing analysis without comparators*
Shi, Honghao, Guo, Wanjie, Zhu, He et al. (2019) Cost-Effectiveness Analysis of Xiyanping Injection (Andrographolide Sulfonate) for Treatment of Adult	- Study does not contain a relevant intervention

Study	Code [Reason]
Community Acquired Pneumonia: A Retrospective, Propensity Score-Matched Cohort Study. Evidence-based complementary and alternative medicine : eCAM 2019: 4510591	*Andrographolide Sulfonate injection*
Shiri, Tinevimbo, Khan, Kamran, Keaney, Katherine et al. (2019) Pneumococcal Disease: A Systematic Review of Health Utilities, Resource Use, Costs, and Economic Evaluations of Interventions. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research 22(11): 1329-1344	- Study does not contain a relevant intervention *Vaccines and antibiotics (not length of treatment)*
Sultana, Marufa, Sarker, Abdur Razzaque, Ali, Nausad et al. (2019) Economic evaluation of community acquired pneumonia management strategies: A systematic review of literature. PloS one 14(10): e0224170	- Study does not contain a relevant intervention *Different antibiotics in adults and bubble continuous positive airway pressure in newborns*
Tesfaye, Solomon H, Loha, Eskindir, Johansson, Kjell Arne et al. (2022) Cost-effectiveness of pulse oximetry and integrated management of childhood illness for diagnosing severe pneumonia. PLOS global public health 2(7): e0000757	- Non OECD country *Ethiopia*
Torres, Antoni, Bassetti, Matteo, Welte, Tobias et al. (2020) Economic analysis of ceftaroline fosamil for treating community-acquired pneumonia in Spain. Journal of medical economics 23(2): 148-155	- Study does not contain a relevant intervention *Different antibiotics not different durations*
Wagner, A P, Enne, V I, Livermore, D M et al. (2020) Review of health economic models exploring and evaluating treatment and management of hospital-acquired pneumonia and ventilator-associated pneumonia. The Journal of hospital infection 106(4): 745-756	- Study does not contain a relevant intervention *Different antibiotics not different durations*
Xie, Xuanqian; Sinclair, Alison; Dendukuri, Nandini (2017) Evaluating the accuracy and economic value of a new test in the absence of a perfect reference test. Research synthesis methods 8(3): 321-332	Included in review question 4.2
Zhang, Shanshan, Sammon, Peter M, King, Isobel et al. (2016) Cost of management of severe pneumonia in young children: systematic analysis. Journal of global health 6(1): 010408	- Study does not contain a relevant intervention *Costing study with no outcomes*