National Institute for Health and Care Excellence

Pneumonia: diagnosis and management (update)

[E] Evidence reviews for corticosteroids as an adjunct to antibiotics in adults with community or hospital acquired pneumonia

NICE guideline [number]

Evidence reviews underpinning recommendations 1.8.1 to 1.8.2 and a research recommendation in the NICE guideline

April 2025

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The clinical and cost-effectiveness of corticosteroid treatment in addition to antibiotic treatment compared with antibiotic treatment alone in adults with CAP

1.1 Review question

In adults with community-acquired pneumonia, what is the clinical and cost effectiveness of corticosteroid treatment in addition to antibiotic treatment, compared with antibiotic treatment alone?

1.1.1 Introduction

It has long been recognised that many pneumonia symptoms are caused by inflammation rather than the causative agents. Corticosteroids are a group of medications whose principal mechanism of action is through suppression of inflammation and these drugs are widely and effectively used in other non-infective disease areas. Unfortunately, it is also recognised that such suppression of inflammation can increase susceptibility to infection and make on-going infections worse. For this reason, there has been reluctance to use corticosteroid treatment widely in the treatment of infection. However, there is some evidence that the addition of a corticosteroid to standard antibiotic therapy at the initiation of treatment can improve outcomes for patients with pneumonia. The safety, efficacy and cost-effectiveness of this remains uncertain.

The aim of this review is to determine the clinical effectiveness and cost-effectiveness of corticosteroids as an adjunctive treatment for community acquired pneumonia (CAP) in hospitalised patients being treated with antibiotics.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	Adult patients (≥18 years old) hospitalized with probable or suspected CAP Exclusion: Predominately (≥80%) patients with Pneumocystis pneumonia, inflammatory cases of pneumonia such as organizing pneumonia, chronic obstructive pulmonary disease (COPD), COVID-19 pneumonia, other viral cases of pneumonia, empyema, post-obstructive pneumonia, or ventilator-associated pneumonia.
Interventions	Antibiotics plus corticosteroids
Comparator	standard care or placebo

Outcomes	• mortality • need for invasive mechanical ventilation • secondary infections • gastrointestinal (GI) bleeding • ICU admission • hyperglycaemia (requiring intervention) • duration of ICU and hospital stay.
Study type	RCTs

CAP= community acquired pneumonia; COPD=chronic obstructive pulmonary disease; GI= gastrointestinal; ICU=intensive care unit

For the full protocol see appendix A.

1.1.3 Methods and process

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

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

Searches for this question identified 4 systematic reviews which matched the inclusion criteria for this review. Of these 4, one systematic review was both recent and a close match:

> Pitre, T., Abdali, D., Chaudhuri, D. et al. Corticosteroids in Community-Acquired Bacterial Pneumonia: a Systematic Review, Pairwise and Dose-Response Meta-Analysis. J GEN INTERN MED 38, 2593–2606 (2023). https://doi.org/10.1007/s11606-023-08203-6

The committee agreed that this review directly addresses the review question, was up to date and thorough, and that it covered all studies included in the previous version of this review (CG191). For this reason, to repeat it would be a duplication of effort. They noted that the searches were last run in September 2022 and that it was possible that newer studies that might be eligible for inclusion could have been published since that time. They asked NICE to update the searches to identify any potential new randomised controlled trials (RCTs) that would affect the results.

The analyses and GRADE were conducted by Pitre 2023 and were not altered by the NICE team. This means that there are minor variations in how the analysis method was used and how GRADE was applied to the findings, compared to standard NICE methods. There are likewise differences in how subgroup analyses were conducted compared to the protocol. Subgroup analysis of treatment duration comparing trials treating for <7 days versus ≥7 days were reported by Pitre 2023 but GRADE was not applied. No additional subgroup analyses were conducted by NICE.

1.1.3.1 Search methods

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

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

The searches for effectiveness evidence were initially run on 12 January 2024. The effectiveness searches were done in three parts so that different date limits and study filters could be applied to the appropriate population:

- RCTs for adults with CAP since September 2022, re-run on 17 October and 20 November 2024;
- any study type for adults with HAP since March 2014, re-run on 20 November 2024;
- and RCTs covering children and young people with CAP or HAP with no date limits, re-run on 18 October and 20 November 2024.

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 and systematic reviews.

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 11 January 2024 using seed references identified from the search for systematic reviews. These were updated on 17 October 2024 using the included studies from the draft of this review.

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. The NICE OECD 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

The searches undertaken for the Pitre (2023) in September 2022 were repeated to identify potentially relevant studies that had been published since the original search. This search found 511 references (see appendix B for the literature search strategy).

These 511 references were screened at title and abstract level against the review protocol, with 503 excluded at this level. 10% of references were screened separately by two reviewers with 100% agreement.

The full texts of 8 RCTs were ordered for closer inspection. 1 of these studies met the criteria specified in the review protocol (appendix A), as a secondary publication of a study reviewed by Pitre (2023). For a summary of the 1 included study from the search and the 18 included studies from Pitre (2023) see Table 3.

A re-run of the search (November 2024) found an additional 275 references. These were screened at title and abstract level and 266 were excluded. The remaining 9 were examined as full texts and 0 met the inclusion criteria specified in the protocol.

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 1: Summary of systematic review included in the effectiveness evidence

Study details	Population	Intervention	Comparison	Outcomes	Risk of bias

Pitre (2023)
Systematic review and meta-analysis
 	
18 Studies
	Total N = 4661
	• Adult patients (≥18 years old)
	• Hospitalized with probable or suspected CAP
	• All severities of disease
		treatment with corticosteroids (all doses, types, and durations) as an adjunct to antibiotics	Usual care with antibiotics
			(including placebo)
				• Mortality
				• Invasive Mechanical Ventilation
				• Need for ICU Admission
				• Duration of Hospitalization
				• Duration of ICU stay
				• Adverse Events:
				  ○ Secondary Infections,
				  ○ Gastrointestinal Bleeding,
				  ○ Hyperglycaemia
				• Ventilator-free days
					Fully applicable
					High risk of bias
					
					Risk of inaccurate findings due to:
					• Errors in transcription of data from primary studies
					• Inconsistent reporting of results
					• Missing detail on outcomes and control conditions
					• Missing risk of bias judgements

CAP=community acquired pneumonia; ICU=intensive care unit

Table 2: Summary of studies included in Pitre (2023) and updated study included from the search

This information is taken from the Pitre (2023) review, except Blum (2023).

Study details	Population	Severity	Intervention	Comparison	Outcomes (risk of bias)
Lloyd (2019) (IMPROVe-GAP trial) Australia	Total N=816 57% male	Non-severe	Prednisone 50mg daily for 7 days[a], + usual care (antibiotic)	Usual care (antibiotic) N=415*	• Duration of hospitalization (high) • Duration of ICU (high)

Study details	Population	Severity	Intervention	Comparison	Outcomes (risk of bias)
	Mean age: 76.1	50% with CORB scores <2 ICU:10.5% Mechanical ventilation: NR	N=401*		• Gastrointestinal bleeding (high) • Hyperglycaemia (high) • ICU admission (high) • Invasive mechanical ventilation (high) • Mortality (high)
Li (2016)* China	Total N= 58 Gender NR Mean age NR	Severe ICU:100% Mechanical ventilation: NR	Methylprednisolone 80mg daily for 7 days[a], + usual care (antibiotic) N= 29*	Usual care (antibiotic) N= 29*	• Duration of hospitalization (high) • Gastrointestinal bleeding (high) • Hyperglycaemia (high) • Secondary infections (high) • Mortality (high)
Nafae (2013) Egypt	Total N= 80 56.2% male Mean age: 49	Severe Mean CORB score>2 ICU: NR Mechanical ventilation: 0%	Hydrocortisone 200mg IV load, then 10 mg/h IV infusion for 7 days, + usual care (antibiotic) N=60	Usual care (antibiotic) N=20	• Duration of hospitalization (high) • Duration of ICU (high) • Gastrointestinal bleeding (high) • Hyperglycaemia (high) • Invasive mechanical ventilation (high) • Mortality (high)
Sabry (2011) Egypt	Total N=80 72.5% male Mean age:62.2	Severe ICU: 100% Mechanical ventilation: 75%	Hydrocortisone 200mg IV load, then 12.5mg/h IV infusion for 7 days, + usual care (antibiotic)	Usual care (antibiotic) N=40	• Gastrointestinal bleeding (low) • Mortality (low)

Study details	Population	Severity	Intervention	Comparison	Outcomes (risk of bias)
			N=40		
Confalonieri (2005) Italy	Total N=46 69.5% male Mean age: 63.5	Severe ICU: 100% Mechanical ventilation: 73.9%	Hydrocortisone 200mg IV load, then 10 mg/h IV infusion for 7 days, + usual care (antibiotic) N=23	Usual care (antibiotic) N=23	• Duration of hospitalization (low) • Duration of ICU (low) • Gastrointestinal bleeding (low) • Hyperglycemia (low) • Secondary infections (low) • Invasive mechanical ventilation (low) • Mortality (low) • Ventilator free days (low)
Mikami (2007) Japan	Total N=31 74.2% male Mean age: 72	Non-severe PSI I-III >50% ICU: 0% Mechanical ventilation: 0%	Prednisolone 40mg IV daily for 3 days, + usual care (antibiotic) N=15	Usual care (antibiotic) N=15	• Duration of hospitalization (high) • Secondary infections (high)
Meijvis (2011) (Ovidius trial) Netherlands	Total N=304 56.5% male Mean age:63.6	Non-severe PSI I-III >50% ICU: 0% Mechanical ventilation: 0%	Dexamethasone 5mg IV daily for 4 days, + usual care (antibiotic) N=151	Usual care (antibiotic) N=153	• Duration of hospitalization (low) • Duration of ICU (low) • Hyperglycaemia (low) • Secondary infections (low) • Mortality (low)
Wittermans (2021) Netherlands	Total N=401 67.4% male Mean age: 67.5	Non-severe PSI I-III >50% ICU: 0%	Dexamethasone 6mg PO daily for 4 days, + usual care (antibiotic)	Usual care (antibiotic) N=198	• Duration of hospitalization (low) • Hyperglycaemia (low) • Mortality (low)

Study details	Population	Severity	Intervention	Comparison	Outcomes (risk of bias)
		Mechanical ventilation: 0%	N=203		
Snijders (2010) Netherlands	Total N=213 58.2% male Mean age: 63.5	Non-severe PSI I-III >50% ICU:10.3% Mechanical ventilation: NR	Prednisolone 40mg daily for 7 days (IV or PO), + usual care (antibiotic) N=104	Usual care (antibiotic) N=109	• Duration of hospitalization (low) • Hyperglycaemia (low) • Secondary infections (low) • Invasive mechanical ventilation (low) • Mortality (low)
El-Ghamrawy (2006) Saudi Arabia	Total N=34 61.8% male Mean age: 61.8	Severe ICU: 100% Mechanical ventilation: NR	Hydrocortisone 200mg IV bolus, then 10mg/h IV infusion for 7 days, + usual care (antibiotic) N=17	Usual care (antibiotic) N=17	• Duration of hospitalization (high) • Secondary infections (high) • Mortality (high) • Gastrointestinal bleeding (not assessed)
McHardy and Schonell (1972) Scotland	Total N=126 48.4% male Mean age: 60.3	Non-severe Mild to moderate ICU: 0% Mechanical ventilation: NR	Prednisolone 5mg every 6 hours for 7 days[a], + usual care (antibiotic) N=40	Usual care (antibiotic) N=86	• Mortality (high)
Fernandez-Serrano (2011) Spain	Total N=45 66.7% male Mean age: 66 for intervention, 61 for control	Severe Fine scores IV-V >50% ICU: 0%	Methylprednisolone 200mg IV bolus, then 20mg IV every 6 hours for 3 days, then 20mg IV every 12 hours for 3 days, then	Usual care (antibiotic) N=22	• Duration of hospitalization (moderate) • Duration of ICU (moderate) • Invasive mechanical ventilation (moderate) • Mortality (moderate)

Study details	Population	Severity	Intervention	Comparison	Outcomes (risk of bias)
		Mechanical ventilation: 0%	20mg IV for 3 days, + usual care (antibiotic) N=23		• Gastrointestinal bleeding (not assessed)
Torres (2015) Spain	Total N=120 61.4% male Mean age: 65.3	Severe PSI IV-V >50% ICU: 75% Mechanical ventilation: 2.5%	Methylprednisolone 0.5mg/kg every 12 hours for 5 days[a], + usual care (antibiotic) N=61	Usual care (antibiotic) N=59	• Duration of hospitalization (low) • Duration of ICU (low) • Gastrointestinal bleeding (low) • Hyperglycaemia (low) • Secondary infections (low) • Invasive mechanical ventilation (low) • Mortality (low)
Blum (2015) and Blum (2023)[+] (STEP trial) Switzerland	Total N=785 62% male Mean age: 74 for intervention, 73 for control	Non-severe PSI I-III >50% ICU: 0% Mechanical ventilation: 0%	Prednisone 5mg PO daily for 7 days, + usual care (antibiotic) N=392	Usual care (antibiotic) N=393	• Duration of hospitalization (low) • Duration of ICU (low) • Gastrointestinal bleeding (low) • Hyperglycaemia (low) • ICU admission (low) • Secondary infections (low) • Invasive mechanical ventilation (low) • Mortality (low)
Marik (1993) UK	Total N=30 NR % male Mean age: 36.44	Severe Apache II score 13 ICU: 100%	Hydrocortisone 10mg/kg IV once, 30 minutes prior to antibiotics + usual care	Usual care (antibiotic) N=16	• Duration of ICU (high) • Invasive mechanical ventilation (high) • Mortality (high)

Study details	Population	Severity	Intervention	Comparison	Outcomes (risk of bias)
		Mechanical ventilation: NR	N=14		
Wagner (1956) USA	Total N=113 67.3% male Mean age: NR	Non-severe ICU:NR Mechanical ventilation: NR	Hydrocortisone PO taper over 5 days (starting with 200mg/day, down to 2mg/day), + usual care (antibiotic) N=52	Usual care (antibiotic) N=61	• Hyperglycaemia (moderate) • Mortality (moderate)
Meduri (2022) (ESCAPe trial) USA	Total N=584 96% male Mean age: 68.8	Severe PSI IV-V >50% ICU: 100% Mechanical ventilation: 33%	Methylprednisolone 40mg IV bolus, then 40mg per day for 7 days, then taper for 20 days, + usual care (antibiotic) N=297	Usual care (antibiotic) N=287	• Duration of hospitalization (low) • Duration of ICU (low) • Gastrointestinal bleeding (low) • Hyperglycaemia (low) • Mortality (low) • Ventilator free days (low) • Secondary infections (not assessed)
Dequin (2023) (CAPE COD trial) France	Total N=795 69.4% male Mean age: 67	Severe PSI IV-V >50% ICU: 100% Mechanical ventilation: 22.2%	Hydrocortisone 2mg IV daily for 4-8 days, + usual care (antibiotic) N=400	Usual care (antibiotic) N=395	• Gastrointestinal bleeding (low) • Secondary infections (low) • Invasive mechanical ventilation (low) • Mortality (low)

CORB= confusion, oxygenation, respiratory rate, and blood pressure; ICU=intensive care unit; IV=intravenous; PSI=pneumonia severity index which is graded on a scale of 1-5

*Information marked with an asterisk was erroneous in Pitre (2023) and has been corrected by NICE.

[+] Blum 2023 is the new publication not included in the Pitre (2023) review
[a] Route of administration not provided by Pitre 2023

See Appendix D for full evidence tables.

1.1.6 Summary of the effectiveness evidence

Table 3: GRADE evidence summary for corticosteroids vs. usual care

This information is taken from the Pitre (2023) review.

Outcomes	N Participants (studies)	Certainty	Relative risk (95% CI)	Anticipated absolute effects	
				Risk with usual care	Risk difference with corticosteroids
Mortality (patients with more severe pneumonia)	2133 (12 RCTs)	Moderate[a]	RR 0.62 (0.45 to 0.85)	146 per 1000	56 fewer per 1000 (81 fewer to 22 fewer)
Mortality (patients with less severe pneumonia)	2434 (7 RCTs)	Low[a,b]	RR 1.08 (0.83 to 1.42)[i]	75 per 1000	6 more per 1000 (13 fewer to 21 more)
Invasive mechanical ventilation	2855 (9 RCTs)	Moderate[a]	RR 0.56 (0.42 to 0.74)	82 per 1000	36 fewer per 1000 (48 fewer to 21 fewer)
ICU admission	2277 (5 RCTs)	Moderate[b]	RR 0.65 (0.43 to 0.97)	51 per 1000	18 fewer per 1000 (29 fewer to 2 fewer)
Duration of hospitalisation	3442 (13 RCTs)	Low[f,g,h]	-	Mean duration = 12.8 days	MD 2.31 days fewer (3.85 fewer to 0.76 fewer)

Outcomes	N Participants (studies)	Certainty	Relative risk (95% CI)	Anticipated absolute effects	
				Risk with usual care	Risk difference with corticosteroids
Duration of ICU stay	926 (9 RCTs)	Low[g,h]	-	Mean duration = 9.9 days	MD 2.06 fewer (3.61 fewer to 0.46 fewer)
Ventilator-free days	630 (2 RCTs)	Moderate[b]	-	Mean duration = 22 days	MD 2.9 days more (0.95 more to 4.85 more)
Secondary infections	2970 (10 RCTs)	Low[b,c]	RR 1.09 (0.85 to 1.41)[j]	77 per 1000	7 more per 1000 (12 fewer to 32 more)
Hyperglycaemia	3362 (11 RCTs)	Moderate[d]	RR 1.76 (1.46 to 2.14)	76 per 1000	58 more per 1000 (35 more to 87 more)
Gastrointestinal bleeding	3368 (11 RCTs)	Low[e]	RR 0.95 (0.56 to 1.60)	17 per 1000	1 fewer per 1000 (8 fewer to 10 more)

[a] Downgraded once for indirectness due to heterogenous definitions of severity
[b] Downgraded once for imprecision because the confidence intervals include MID
[c] Downgraded once for indirectness due to heterogenous definition of infections
[d] Downgraded once for indirectness because the outcome of interest was hyperglycaemia requiring intervention, but most trials reported only hyperglycaemia
[e] Downgraded once for imprecision because the confidence intervals cross the MID in both directions
[f] Downgraded once for risk of bias due to statistically significant subgroup effect, with the most benefit from high risk of bias trials
[g] Downgraded once for inconsistency due to critical heterogeneity
[h] Downgraded once for risk of bias because although there was no statistically significant difference in subgroups of risk of bias, most of the benefit is derived from three high risk of bias trials
[i] 180 day results from the STEP trial (Blum 2023) were consistent with the 30 day results included in this analysis, showing no significant difference between corticosteroids and usual care. Therefore, the updated numbers are unlikely to significantly alter the direction or magnitude of the pooled result.
[j] 180 day results from the STEP trial (Blum 2023) differed from the 30 day results included in this analysis. The 180 days follow up showed a significant effect favouring usual care, whereas the 30 day follow up showed no significant difference. Based on the overall pattern of results in the meta-analysis (see Forest plots in Appendix E), this is unlikely to significantly alter the direction or magnitude of the pooled result.

Table 5: Evidence summary of subgroup analysis for corticosteroids vs. usual care, by duration of treatment <7 days versus ≥7 days

This information is taken from the Pitre (2023) review. GRADE was not applied to these findings by Pitre (2023).

Outcomes	N Participants (studies)	Certainty	Relative risk (95% CI) / mean difference (95%CI) <7 days	Relative risk (95% CI) / mean difference (95%CI) ≥7 days	P-value[a] of group difference
Mortality (more severe pneumonia)	2133 (12 RCTs)	Not assessed	RR 0.62 (0.45 to 0.87)	RR 0.8 (0.57 to 1.13)	p=0.3; not significant
Invasive mechanical ventilation	2855 (9 RCTs)	Not assessed	RR 0.6 (0.43 to 0.84)	RR 0.48 (0.29 to 0.78)	p=0.46; not significant
ICU admission	2277 (5 RCTs)	Not assessed	RR 0.51 (0.25 to 1.02)	RR 0.74 (0.45 to 1.21)	p=0.39; not significant
Duration of hospitalisation	3442 (13 RCTs)	Not assessed	MD -0.94 (-1.6 to -0.29)	MD -2.74 (-4.85 to -0.63)	p=0.11; not significant
Duration of ICU stay	926 (9 RCTs)	Not assessed	MD -0.61 (-1.94 to 0.73)	MD -2.95 (-5.07 to -0.83)	p=0.07; not significant

[a] p-value threshold for significance set at p<0.05

See appendix F for full GRADE tables.

1.1.7 Economic evidence

1.1.7.1 Included studies

A single search was performed to identify published economic evaluations of relevance to any of the questions in this guideline update. See 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. See Appendix G – Economic evidence study selection for the study selection process.

1.1.7.2 Excluded studies

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

1.1.8 Summary of included economic evidence

No health economic evidence included.

1.1.9 Economic model

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

1.1.10 Unit Costs

To better understand the impact of using corticosteroids, unit cost data was obtained for different corticosteroid treatments. Table 6: Unit cost shows the unit costs of the treatments found in the effectiveness review and Table shows the most commonly used treatments identified by the committee and the total costs per patient over the course of treatment.

Table 6: Unit costs for corticosteroids

Treatment and dose or continuous infusion	Unit cost per dose	Source
Prednisone 40mg PO	£0.21	BNF 2024
Methylprednisolone 200mg IV	£9.50	BNF 2024
Methylprednisolone 80mg IV	£3.16	BNF 2024
Methylprednisolone 20mg IV	£1.58	BNF 2024
Hydrocortisone 200mg IV	£1.83	BNF 2024
Hydrocortisone 10mg/h IV continuous infusion	£2.76	BNF 2024
Hydrocortisone 12.5mg/h IV continuous infusion	£2.76	BNF 2024
Dexamethasone 6mg PO	£4.28	BNF 2024

Table 7: Total costs for most common treatments

Treatment/regimen	Duration of treatment/regimen	Total cost per patient
Hydrocortisone 200mg IV bolus (first day), then 10mg/h IV infusion (following 6 days)	7 days	£18.39 (£1.83+6*2.76)
Dexamethasone 6mg PO	7 days	£29.96 (7*4.28)

1.1.11 Evidence statements

An RCT (n=785) follow up study by Blum (2023) provided 180 day follow-up outcomes for the STEP trial for mortality and secondary infections (reported in Blum 2015). This evidence was rated directly applicable and at low risk of bias.

- For mortality, the 180 day results were consistent with the 30 day results, showing no significant difference between corticosteroids and usual care. Mortality for usual care = 25/366 (6.8%), corticosteroids = 35/361 (9.7%), RR 1.42 (0.87–2.32), P=0.601.
- For secondary infections, 180 day results differed from the 30 day results. The 30 day results showed no significant difference between groups, whereas the 180 day results showed a significant effect favouring usual care, rather than corticosteroids. Secondary infections for usual care = 35/366 (9.6%), corticosteroids = 62/361 (17.2%) RR 1.78 (1.22–2.54), P=0.003.

1.1.12 References – included studies

1.1.12.1 Effectiveness

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Blum CA, Nigro N, Briel M, Schuetz P, Ullmer E, Suter-Widmer, I, et al. (2015) Adjunct prednisone therapy for patients with community acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. The Lancet. 385(9977): 1511-8

Marik P, Kraus P, Sribante J, Havlik I, Lipman J, Johnson DW. (1993) Hydrocortisone and tumor necrosis factor in severe community acquired pneumonia: a randomized controlled study. Chest. 104(2): 389-92

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Meduri GU, Shih MC, Bridges L, Martin TJ, El-Solh A, Seam N, et al. (2022) Low-dose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. Intensive Care Med. 48(8): 1009-23

Dequin PF, Meziani F, Quenot J, Kamel T, Jean-Damien R, Badie J, Amélie L. G. (2023). Hydrocortisone in severe community-acquired pneumonia. *The New England Journal of Medicine, 388*(21): 1931-1941

1.1.12.2 Economic

No economic studies were included however unit cost were from:

National Institute for Health and Care Excellence (2024) BNF, https://bnf.nice.org.uk/ Accessed: 8th August 2024

The clinical and cost-effectiveness of corticosteroid treatment in addition to antibiotic treatment compared with antibiotic treatment alone in adults with HAP

1.2 Review question

In adults with hospital-acquired pneumonia, what is the clinical and cost effectiveness of corticosteroid treatment in addition to antibiotic treatment, compared with antibiotic treatment alone?

1.2.1 Introduction

Many pneumonia symptoms may be caused by inflammation rather than the causative agents. Corticosteroids are a group of medications whose principal mechanism of action is through suppression of inflammation and these drugs are widely and effectively used in other non-infective disease areas. Unfortunately, it is also recognised that such suppression of inflammation can increase susceptibility to infection and make on-going infections worse. There has been reluctance to use corticosteroid treatment widely in the treatment of infection. However, there is some evidence that the addition of a corticosteroid to standard antibiotic therapy at the initiation of treatment can improve outcomes for patients with pneumonia. The safety, efficacy and cost-effectiveness of this remains uncertain.

The aim of this review is to determine the clinical effectiveness and cost-effectiveness of corticosteroids as an adjunctive treatment for hospital acquired pneumonia (HAP) in hospitalised patients being treated with antibiotics.

1.2.2 Summary of the protocol

Table 8: PICOS inclusion criteria

Population	Adults (≥18 years) with hospital-acquired pneumonia 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: • 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 witnessed aspiration pneumonia as a result of inhaling a bolus of gastric contents.
Interventions	Antibiotic plus corticosteroid
Comparator	Antibiotic plus placebo or antibiotic alone

Outcomes	Primary outcomes:
	• Mortality – all cause and disease specific (at 30 days)
	• Need for invasive ventilation (in those not requiring invasive ventilation at baseline)
	• ICU / ITU admission (in those not requiring ICU/ITU admission at baseline)
	• Duration of hospital stay/duration of ICU stay
	• Clinical cure/clinical stability at the end of follow up.
	• Adverse events, including:
	  ○ Gastrointestinal bleeding
	  ○ Hyperglycaemia (requiring intervention)
	  ○ Complications (composite of empyema, effusion, abscess, metastatic infection, superinfection, MODS, bacteraemia)

Study type	Systematic reviews of RCTs and RCTs

For the full protocol see appendix A.

1.2.3 Methods and process

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

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

1.2.3.1 Search methods

The searches for systematic reviews on all pneumonia topics published since 2014 were run on 20 November 2023 in Cochrane Database of Systematic Reviews (CDSR) (Wiley) and Epistemonikos (https://www.epistemonikos.org).

The searches for effectiveness evidence were run on 12 January 2024. The effectiveness searches were done in three parts so that different date limits and study filters could be

applied to the appropriate population (RCTs for adults with CAP since September 2022; any study type for adults with HAP since March 2014; and RCTs covering children and young people with CAP or HAP with no date limits).

The following databases were searched: Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley); Embase (Ovid); and MEDLINE ALL (Ovid). Limits were applied to remove animal studies, editorials, conference abstracts, empty registry entries and papers not published in the English language. Validated filters were used in MEDLINE and Embase to remove records about non-OECD countries and to limit to RCTs and systematic reviews.

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 11 January 2024 using seed references identified from the search for systematic reviews.

The searches for cost effectiveness evidence were run on 20 November 2023 for papers published since 2014. The following databases were searched: Econlit (Ovid); Embase (Ovid); International HTA Database (INAHTA) (https://database.inahta.org); and MEDLINE ALL (Ovid). The validated NICE Cost Utility Filter was used on MEDLINE and Embase.

A NICE information specialist conducted the searches. The MEDLINE strategy was quality assured by a trained NICE information specialist 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.

1.2.4 Effectiveness evidence

1.2.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 295 references (see appendix B for the literature search strategy).

These 295 references were screened at title and abstract level against the review protocol, with 291 excluded at this level. 10% of references were screened separately by two reviewers with 100% agreement.

The full texts of 4 RCTs were ordered for closer inspection. None of these studies met the criteria specified in the review protocol (appendix A).

A re-run of the search (November 2024) found an additional 64 references. These were screened at title and abstract level and 64 were excluded. No full texts were examined.

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

1.2.4.2 Excluded studies

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

1.2.5 Summary of studies included in the effectiveness evidence

No evidence identified.

1.2.6 Economic evidence

1.2.6.1 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. See Appendix G – Economic evidence study selection for the study selection.

1.2.6.2 Excluded studies

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

1.2.7 Summary of included economic evidence

No health economic evidence included.

1.2.8 Economic model

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

1.2.9 Unit Costs

To better understand the impact of using corticosteroids, unit cost data was obtained for different corticosteroid treatments. Table 6: Unit cost shows the unit costs of the treatments found in the effectiveness review and Table shows the most commonly used treatments identified by the committee and the total costs per patient over the course of treatment.

Table 9: Unit costs for corticosteroids

Treatment and dose or continuous infusion	Unit costs per dose	Source
Prednisone 40mg PO	£0.21	BNF 2024
Methylprednisolone 200mg IV	£9.50	BNF 2024
Methylprednisolone 80mg IV	£3.16	BNF 2024
Methylprednisolone 20mg IV	£1.58	BNF 2024
Hydrocortisone 200mg IV	£1.83	BNF 2024
Hydrocortisone 10mg/h IV continuous infusion	£2.76	BNF 2024

Treatment and dose or continuous infusion	Unit costs per dose	Source
Hydrocortisone 12.5mg/h IV continuous infusion	£2.76	BNF 2024
Dexamethasone 6mg PO	£4.28	BNF 2024

1 **Table 10: Total costs for most common treatments**

Treatment/regimen	Length of treatment/regimen	Total cost per patient
Hydrocortisone 200mg IV bolus (first day), then 10mg/h IV infusion (following 6 days)	7 days	£18.39 (£1.83+6*2.76)
Dexamethasone 6mg PO	7 days	£29.96 (7*4.28)

2

The clinical and cost-effectiveness of corticosteroid treatment in addition to antibiotic treatment compared with antibiotic treatment alone in children with CAP or HAP

1.3 Review question

In children and young people with hospital- or community-acquired pneumonia, what is the clinical and cost effectiveness of corticosteroid treatment in addition to antibiotic treatment, compared with antibiotic treatment alone?

1.3.1 Introduction

It has long been recognised that many pneumonia symptoms are caused by inflammation rather than the causative agents. Corticosteroids are a group of medications whose principal mechanism of action is through suppression of inflammation and these drugs are widely and effectively used in other non-infective disease areas. Unfortunately, it is also recognised that such suppression of inflammation can increase susceptibility to infection and make on-going infections worse. For this reason, there has been reluctance to use corticosteroid treatment widely in the treatment of infection. However, there is some evidence that the addition of a corticosteroid to standard antibiotic therapy at the initiation of treatment can improve outcomes for patients with pneumonia. The safety, efficacy, and cost-effectiveness of this remains uncertain.

1.3.2 Summary of the protocol

Table 11: PICOS inclusion criteria

Population	Inclusion: Babies over 28 days (corrected gestational age), children, young people (age <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). • Babies, children and young people with COVID-19 pneumonia. • Babies, children and young people who acquire pneumonia while intubated (ventilator-associated pneumonia).

	• Babies, children and young 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). • Babies, children and young people in whom pneumonia is an expected terminal event. • Babies, children and young people with non-pneumonic infective exacerbations of bronchiectasis. • Babies, children and young people with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • Babies, children and young people with pneumonia associated with cystic fibrosis. • Babies, children and young people with witnessed/known aspiration pneumonia as a result of inhaling a bolus of gastric contents.
Interventions	Antibiotic plus corticosteroid for CAP Antibiotic plus corticosteroid for HAP Notes: • all antibiotics will be pooled • all corticosteroids will be pooled. • route of administration for antibiotic may be oral or intravenous and for corticosteroid may be oral, intravenous or by inhalation
Comparator	Antibiotic plus placebo or antibiotic alone

Outcomes	• Mortality – all cause and disease specific (at 30 days)
	• Need for invasive ventilation (in those not requiring invasive ventilation at baseline)
	• ICU / ITU admission (in those not requiring ICU/ITU admission at baseline)
	• Duration of hospital stay, duration of ICU stay, escalation of care
	• Clinical cure/clinical stability at the end of follow up.
	• Adverse events, including:
	  ○ Gastrointestinal bleeding
	  ○ Hyperglycaemia
	  ○ Complications (composite of empyema, effusion, abscess, metastatic infection, superinfection, MODS, Bacteraemia)

Study type	Systematic reviews of RCTs and RCTs.

For the full protocol see appendix A.

1.3.3 Methods and process

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

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

The protocol planned to conduct subgroup analysis if heterogeneity is present in the results. Although this was the case, the committee agreed that further analysis would not be valuable due to the low applicability of the evidence.

1.3.3.1 Search methods

The searches for systematic reviews on all pneumonia topics published since 2014 were run on 20 November 2023 in Cochrane Database of Systematic Reviews (CDSR) (Wiley) and Epistemonikos (https://www.epistemonikos.org).

The searches for effectiveness evidence were run on 12 January 2024 and re-run on November 2024. The effectiveness searches were done in three parts so that different date limits and study filters could be applied to the appropriate population (RCTs for adults with CAP since September 2022; any study type for adults with HAP since March 2014; and RCTs covering children and young people with CAP or HAP with no date limits).

The following databases were searched: Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley); Embase (Ovid); and MEDLINE ALL (Ovid). Limits were applied to remove animal studies, editorials, conference abstracts, empty registry entries and papers not published in the English language. Validated filters were used in MEDLINE and Embase to remove records about non-OECD countries and to limit to RCTs and systematic reviews.

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 11 January 2024 using seed references identified from the search for systematic reviews.

The searches for cost effectiveness evidence were run on 20 November 2023 for papers published since 2014. The following databases were searched: Econlit (Ovid); Embase (Ovid); International HTA Database (INAHTA) (https://database.inahta.org); and MEDLINE ALL (Ovid). The validated NICE Cost Utility Filter was used on MEDLINE and Embase.

A NICE information specialist conducted the searches. The MEDLINE strategy was quality assured by a trained NICE information specialist 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.

1.3.4 Effectiveness evidence

1.3.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 834 references (see appendix B for the literature search strategy).

These 834 references were screened at title and abstract level against the review protocol, with 792 excluded at this level. 10% of references were screened separately by two reviewers with 100% agreement.

The full texts of 42 RCT's were ordered for closer inspection. 5 of these studies met the inclusion criteria specified in the review protocol (appendix A). For a summary of the 5 included studies see table 2.

A re-run of the search found an additional 168 references. These were screened at title and abstract level and 160 were excluded. The remaining 8 were examined as full texts and 0 met the inclusion criteria specified in the protocol.

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

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

1.3.4.2 Excluded studies

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

1.3.5 Summary of studies included in the effectiveness evidence

Table 12: Summary of studies included in the effectiveness evidence

Study details	Setting and location	Population	Intervention	Comparison	Risk of bias
Kun 2018 RCT Follow up time: 3 weeks	Shanghai Children's Hospital China	N=100 Children with mycoplasma pneumonia	N=50 Methylprednisolone (5% GS) IV 1 mg / kg daily. When body temperature normalized, this was switched to oral methylprednisolone 1 mg / kg orally daily. Azithromycin (5% GS) IV 10 mg / kg daily. When the body temperature normalized, this was switched to oral azithromycin 10 mg / kg daily.	N=50 Azithromycin (5% GS) IV 10 mg / kg daily. When the body temperature normalized, this was switched to oral azithromycin 10 mg / kg daily.	Moderate
Nagy 2013 RCT Follow up time:5 days	University of Debrecen Hungary	N=59 Children with severe CAP	N=29 Methylprednisolone 0.5–2.0 mg/kg for 5 days, + antibiotics: Imipenem IV 60 mg/body weight kg for >= 7 days	N=30 5% dextrose as placebo, + antibiotics: Imipenem IV 60 mg/body weight kg for >= 7 days	Moderate
Shan 2017 RCT Follow up time:7 days	Shengjing Hospital of China Medical University China	N=151 Children with refractory Mycoplasma pneumoniae pneumonia (RMPP)	N=56 IV methylprednisolone 2 mg/kg/day + IV azithromycin 10 mg/kg/ day, for 3 days	N=56 IV azithromycin 10 mg/kg/ day for 3 days	High

Study details	Setting and location	Population	Intervention	Comparison	Risk of bias
Taggaro 2017 RCT Follow up time: Not reported	Tertiary care, teaching hospitals Spain	N= 60 Children with CAP and pleural effusion. Age range: 1 month to 14 years	N=30 IV dexamethasone 0.25 mg/kg every 6 hours over 48 hours, plus antibiotics (ranitidine concomitantly and cefotaxime until 48 hours after the patient was afebrile, followed with co-amoxyclav).	N=30 Placebo every 6 hours over 48 hours, plus antibiotics (ranitidine concomitantly and cefotaxime until 48 hours after the patient was afebrile, followed with co-amoxyclav).	Low
Wang 2022 RCT Follow up time: Not reported	Zhejiang Provincial People's Hospital China	N=60 Children with Mycoplasma Pneumoniae Pneumonia (MPP)	N=30 Methylprednisolone 2.0 mg/kg for 5 days (route of administration not reported). Erythromycin IV 15 mg/kg once every 12 hours for 5 days. Then no treatment for 4 days, then Azithromycin orally 10 mg/kg for 5 days.	N= 30 Erythromycin IV 15 mg/kg once every 12 hours for 5 days. Then no treatment for 4 days, then Azithromycin orally 10 mg/kg for 5 days.	Moderate

CAP=community acquired pneumonia; IA=intravenous azithromycin; MA=macrolide antibiotics; MPP=mycoplasma pneumoniae pneumonia; RCT=randomised controlled trial; RMPP=refractory mycoplasma pneumoniae pneumonia

See appendix D for full evidence tables

1..6 Summary of the effectiveness evidence

Table 13: Summary of findings table for corticosteroids + antibiotics compared to antibiotics +/- placebo for pneumonia in children and young people

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Interpretation of effect
				Risk with antibiotics +/- placebo	Risk with Corticosteroids + antibiotics	
Cure (all participants with mycoplasma pneumonia, follow up time not specified)	160 (2 RCTs)[a]	Low[b,c]	RR 1.36 (0.93 to 1.98)	350 per 1,000	476 per 1,000 (326 to 693)	Could not differentiate
Any adverse events - total	217 (3 RCTs)[d]	Very low[b,e,f]	RR 0.60 (0.46 to 0.80)	642 per 1,000	385 per 1,000 (295 to 514)	Favours corticosteroids
Average febrile period (days, all participants with refractory mycoplasma pneumonia)	102 (1 RCT)[g]	Very low[h,i]	-	Mean average 7 days (SD 0.35)	Mean average 0.86 days (SD 0.85)	Favours corticosteroids
All cause mortality (parapneumonic effusion, follow up time not specified)	58 (1 RCT)[j]	Very low[i,k]	RR 0.75 (0.18 to 3.06)	138 per 1,000	103 per 1,000 (25 to 422)	Could not differentiate
Progression of simple effusion requiring pleural drainage (parapneumonic effusion, days 1-3)	58 (1 RCT)[j]	Very low[i,k]	RR 0.33 (0.04 to 3.02)	103 per 1,000	34 per 1,000 (4 to 312)	Could not differentiate
Time to recovery (all participants with parapneumonic effusion)	60 (1 RCT)[j]	Low[i,l]	-	Median average 177 hours (115 to 238)	Median average 109 hours (37 to 180)	Favours corticosteroids

Length of hospital stay (days, all participants with mycoplasma pneumonia)	160 (2 RCTs)[a]	Moderate[b]	-	Mean average 11.55 days (SD 2.78)	Mean average 7.51 days (SD 2.27)	Favours corticosteroids

a. Kun 2018, Wang 2022
b. Downgraded once as greater than 33.3% of the weight in the meta-analysis came from studies at moderate or high risk of bias
c. Downgraded once as 95%CI crosses one clinical decision threshold (1.25)
d. Kun 2018, Nagy 2013, Tagarro 2017
e. Downgraded twice as the I2 was greater than 66.7% (I2 = 87%)
f. Downgraded once as 95%CI crosses one clinical decision threshold (0.8)
g. Shan 20117
h. Downgraded twice for serious risk of bias: major limitation of the trial was its "open" design, thus cross-contamination cannot be ruled out. Because there is no placebo control group, a placebo effect cannot be excluded.
i. Downgraded once for inconsistency: single study
j. Tagarro 2017
k. Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)
l. Downgraded once for moderate risk of bias

See appendix F for full GRADE tables.

1.3.7 Economic evidence

1.3.7.1 Included studies

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

This search retrieved 3,201 studies. Based on title and abstract screening, 3,168 of the studies could confidently be excluded for this question. Thirty-three studies were excluded following the full-text review. See **Error! Reference source not found.** for the study selection process.

1.3.7.2 Excluded studies

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

1.3.8 Summary of included economic evidence

There are no included studies in this review question.

1.3.9 Economic model

No original economic modelling was completed for this review question.

1.3.10 Unit costs

No unit costs were supplied for this review question.

1.2.10 References – included studies

1.2.10.1 Effectiveness

Kun, J.; Chao, W.; Silei, Y. (2018) Effect of combination of methylprednisolone and azithromycin on pediatric mycoplasma pneumonia and its effects on procalcitonin, hs-crp, cardiac troponin and il-2. Acta Medica Mediterranea 34(3): 805-809

Nagy, Bela, Gaspar, Imre, Papp, Agnes et al. (2013) Efficacy of methylprednisolone in children with severe community acquired pneumonia. Pediatric pulmonology 48(2): 168-75

Shan, L.-S., Liu, X., Kang, X.-Y. et al. (2017) Effects of methylprednisolone or immunoglobulin when added to standard treatment with intravenous azithromycin for refractory Mycoplasma pneumoniae pneumonia in children. World Journal of Pediatrics 13(4): 321-327

Tagarro, Alfredo, Otheo, Enrique, Baquero-Artigao, Fernando et al. (2017) Dexamethasone for Parapneumonic Pleural Effusion: A Randomized, Double-Blind, Clinical Trial. The Journal of pediatrics 185: 117-123e6

Wang, J. and Zhang, Y. (2022) THE EFFECT OF METHYLPREDNISOLONE COMBINED WITH MACROLIDE ANTIBIOTICS ON MYCOPLASMA PNEUMONIAE PNEUMONIA IN CHILDREN. Farmacia 70(5): 850-854

The committee's discussion and interpretation of the evidence

1.4 The committee's discussion and interpretation of the evidence

1.4.1 The outcomes that matter most

Adults

The committee agreed that mortality was the most important outcome, especially for patients with severe pneumonia. They stated that reducing mortality (within 30 days), in addition to reducing time in hospital and reducing time in ICU, would indicate a clear reason to recommend using corticosteroids as an adjunct to antibiotics in patients with severe pneumonia.

The committee were particularly interested in the findings on ICU admission, particularly for patients with less severe pneumonia. They also focused on whether for patients overall, corticosteroids reduced the need for mechanical ventilation. They felt these were important outcomes because preventing the need to escalate treatment is an important goal for the individual person's care and doing so successfully could have wider benefits for resource allocation.

The committee were concerned about adverse effects of corticosteroids as these outcomes informed the balance of benefits and harms that was critical to their decision on whether to recommend them. They were particularly interested in hyperglycaemia and secondary infections in less severe populations.

Babies, children, and young people

The committee agreed that mortality was the most important outcome, they were specifically concerned with this outcome for babies, children and young people with severe pneumonia. Outcomes such as length of hospital stay, clinical cure and average febrile period were also considered important as they are markers of treatment success and may have wider benefits relating to resource allocation. The committee were concerned about the potential adverse effects of corticosteroids, and as this would inform the balance of benefits and harms that is critical to their decision on whether to recommend them, these were also considered important outcomes.

1.4.2 The quality of the evidence

Adults

The included systematic review, Pitre (2023) applied GRADE to their findings and determined that 4 findings were of moderate confidence (invasive mechanical intervention, ICU admission, ventilator-free days, and hyperglycaemia) and 5 findings were of low confidence (mortality, duration of hospitalisation, duration of ICU, secondary infections, and gastrointestinal bleeding). One of the main reasons for downgrading across all findings was that the studies used heterogeneous definitions of severity. This meant that almost all findings were downgraded at least once for

indirectness on this basis because severity was used to define the subgroups used in most comparisons.

The committee agreed that overall, the included studies in the review (and the additional study) provided good quality evidence from a substantial evidence base. They acknowledged that Pitre (2023) was at high risk of bias and were made aware of the problems in the review with errors in the transcription of data from primary studies, inconsistent reporting of results, missing detail on outcomes and control conditions, and missing risk of bias judgements. Nonetheless, the committee were satisfied that these were minor errors that did not affect the direction or magnitude of the outcomes and that none of the problems identified with the review substantially undermined its findings or prevented it being used as a source of evidence.

The searches carried out for hospital acquired pneumonia (HAP) in adults found no eligible results, so there is a gap in the evidence in this area.

Babies, children, and young people

There was no evidence identified for children and young people with hospital acquired pneumonia (HAP); the evidence was limited to community acquired pneumonia (CAP) only. The quality of the evidence was assessed for each outcome using GRADE, with findings ranging from very low to moderate confidence in the evidence. The main reasons for downgrading were risk of bias, inconsistency, and imprecision.

There were significantly fewer adverse effects for mycoplasma pneumonia and severe CAP when using corticosteroids, but no difference for parapneumonic effusion. The committee noted this very serious inconsistency and acknowledged that the Tarrago (2017) study of children with CAP and parapneumonic effusion differed from the other 2 studies. The committee considered the applicability of this study population and acknowledged that parapneumonic effusions are common enough that the study was useful for this review, particularly because of the limited number of eligible studies identified and overall paucity of relevant evidence. Similarly, the committee noted that 3 of the 5 included studies were based on children with mycoplasma pneumoniae (MP), which is an atypical bacterial pneumonia that may not respond well to the usual first line antibiotics and often shows a more prolonged time course than pneumonias caused by other pathogens. Mycoplasma pneumoniae may also have an autoimmune element so may respond to corticosteroids differently to other pathogens.

The committee concluded that there was only one remaining study in this review that looked at undifferentiated pneumonia in children and was most applicable to ‘typical’ pneumonias seen in children rather than pneumonias with pleural effusion or mycoplasma strains. As this most relevant study did not report any of the main outcomes of interest and only provided data on adverse events, the committee concluded that the evidence was weak and did not sufficiently answer the review question. The committee also noted that the choice of antibiotic in the studies was not consistent with those commonly used in the UK, particularly azithromycin which is not licenced for use with children and imipenem which would not normally be used to treat a child with pneumonia. This further reduced the applicability of the evidence.

1.4.3 Benefits and harms

Adults

The committee acknowledged the possible harms from use of corticosteroids, including both the evidence of harm found in the evidence of increased hyperglycaemia, and also other known risks with corticosteroids, such as hypertension.

They discussed the difference in risk for people with low severity and high severity pneumonia and agreed that for people with high severity pneumonia, the benefits in terms of reduced mortality outweighed the risk of other adverse effects. This reasoning underlined their decision to recommend the use of corticosteroids for people with severe pneumonia.

For less severely ill people, they discussed the risk of longer-term adverse events, referring to the 180 day follow up study of the STEP trial by Blum (2023). Blum had previously found no difference in the number of patients with a secondary infection at 30 day follow-up, but at 180 day follow up they found increased infections in the group who were given corticosteroids. The committee considered whether this indicated a risk that developed over the longer term, which may not be apparent in the meta-analysis which used mixed follow-up times (closest to 90 days).

The committee discussed these risks in comparison to usual practice for other clinical conditions. They noted that corticosteroids are given routinely for many conditions despite the risks, so it would be consistent to also offer them for all severities of pneumonia in the same way. They concluded, however, that as the clearest benefit was for patients with more severe pneumonia, there was insufficient justification to accept these risks for patients with less severe pneumonia. For this reason, they decided that they should not make a recommendation for people with less severe pneumonia. The quantity and quality of the evidence presented for adults was sufficient, so the committee did not choose to make a research recommendation for people with less severe pneumonia as they did not think more evidence would make enough difference to alter their conclusions. They did, however, decide that more information on dose, duration and route of administration for corticosteroids, as well as the pathogen involved would be helpful across the full spectrum of severity, so chose instead to focus a research recommendation on these factors.

Babies, children, and young people

The committee considered the evidence from a study of patients with parapneumonic effusions and agreed that in that study corticosteroids did not reduce the risk of all-cause mortality in children and young people compared to placebo. No other studies reported outcome data for mortality. There was also no difference in rate of cure or disease progression (from simple effusion to requiring drainage in patients with parapneumonic effusion) in patients receiving corticosteroids compared to patients given placebo. The committee noted that length of hospital stay, average febrile period, and time to recovery was significantly reduced in patients receiving corticosteroids compared to patients given placebo, but these findings were limited to patients with mycoplasma pneumoniae and parapneumonic effusions, respectively.

The evidence showed that patients receiving corticosteroids reported significantly fewer adverse events than patients given placebo, and the committee considered this finding in combination with the evidence for a more rapid resolution of symptoms and shorter hospital stays. They reflected on the evidence for the use of corticosteroids in adult patients with pneumonia and the positive recommendation that arose from this evidence, and they considered whether this could be extrapolated to children. However, given the weak evidence base and limited applicability of the included

trials, the committee agreed that it did not currently support a recommendation on the use of corticosteroids for children with pneumonia.

1.4.4 Cost effectiveness and resource use

Adults

There was no existing health economic evidence for this review question. The committee noted that steroids (in addition to antibiotics) are a low cost (Table 9 and Table10) and effective treatment option with acceptable levels of adverse effects in people with severe community-acquired pneumonia. The committee noted the reduced mortality, as well as the reduction of 2,31 days in hospital, 2.03 days in ICU and 2.9 more ventilator free days. Therefore, they are likely to be cost-effective in this sub-group. However, in people with less severe pneumonia, the benefits were less clear and also there was evidence of potential harms, mainly hyperglycaemia, which can result in significant costs.

Currently, steroids are not routinely used for treating bacterial pneumonia. Therefore, their use in people with severe community-acquired pneumonia may result in a slight increase in costs. However, this increase is unlikely to be significant and is likely to be outweighed by improved outcomes. Additionally, using steroids can lead to cost savings by preventing complications and reducing the number of hospital days, days in the ICU, and days on a ventilator. Therefore, it is unlikely that the recommendations will have a significant resource impact.

Babies, children, and young people

There was no existing cost effectiveness evidence for this review question, and as the effectiveness evidence was uncertain, the committee decided not to make any recommendations for children and young people. Therefore, there will not be a resource impact.

1.4.5 Other factors the committee took into account

Adults

The committee noted that the evidence overall indicated a benefit to using corticosteroids and were able to make a recommendation for using a corticosteroid alongside antibiotics. They further discussed the subgroups within the Pitre (2023) findings and the indication from these that hydrocortisone may be more effective, though a direct comparison between the different corticosteroids was not undertaken. Discussing this alongside their expertise and practice considerations the committee agreed a recommendation to consider using IV hydrocortisone initially if choosing a corticosteroid, based on the available evidence, ability to prescribe intravenously and potential issues with oral administration in patients with severe illness.

The committee discussed evidence comparing shorter (<7 days) to longer (>=7 days) of corticosteroids and noted there was little difference, however they agreed that in their clinical experience, shorter courses were preferred to minimise the possible adverse effects.

The committee also noted that some antibiotic and corticosteroid combinations should not be used together. Notes were added below the recommendations to note

that the use of some corticosteroids will be off label, and a note to check MHRA advice on the coadministration of fluoroquinolone antibiotics and corticosteroids.

Whilst the committee was able to make a recommendation on the use of corticosteroids as adjuncts to antibiotics for people hospitalised with CAP based on the limited evidence available and their expertise, they agreed that this was a promising area of research and wished to make a research recommendation to further strengthen the evidence. They also wished to expand the research to people with HAP and babies, children, and young people with HAP or CAP and included these populations in the research recommendation.

Appendices

Appendix A – Review protocols

Review protocol for RQ6.1a Community-acquired pneumonia in adults

Review protocol for RQ6.1b Hospital-acquired pneumonia in adults

Review title	In adults with community or hospital-acquired pneumonia, what is the clinical and cost effectiveness of corticosteroid treatment in addition to antibiotic treatment, compared with antibiotic treatment alone?
Review question	In adults with community or hospital-acquired pneumonia, what is the clinical and cost effectiveness of corticosteroid treatment in addition to antibiotic treatment, compared with antibiotic treatment alone?
Objective	To understand the potential clinical and economic risks and benefits of corticosteroids as an adjunctive treatment for CAP or HAP in hospitalised patients being treated with antibiotics.
Searches	There will be separate searches for the effectiveness and cost effectiveness evidence. **Sources for effectiveness evidence** There will be a combined search for systematic reviews covering all review questions in this guideline. This 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.

	The following databases will be searched for the effectiveness evidence: • 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. The following sources will be applied as required to ensure relevant records are not missed: • The reference lists of potentially relevant systematic reviews will be checked. • The references lists of any key potentially relevant publications will be checked where appropriate to the parameters set out in sections 6-10 below. • Later citations of any key trials or protocols identified in the search results could be checked where appropriate to the parameters set out in sections 6-10 below. • The guideline committee or other stakeholders could be asked if they are aware of any other relevant studies that could be considered. The searches for effectiveness evidence will be conducted from the date of the last search. **Sources 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). **Managing 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. 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]).

	With the agreement of the guideline committee, the searches will be re-run 6-8 weeks before final submission of the review and further studies retrieved for inclusion. The information services team at NICE will quality assure the principal search strategy and peer review the other strategies. Any revisions or additional steps will be agreed by the review team before being implemented. The full search strategies for all databases will be published in the final review.
Condition or domain being studied	Community and hospital-acquired pneumonia
Population	**For CAP only** A SR has been identified by Pitre et al 2023 that will provide the evidence for the CAP element of this RQ. Inclusion 1. Adult patients (≥18 years old) hospitalized with probable or suspected CAP Exclusion: Trials that enrolled predominately (≥80%) patients with Pneumocystis jirovecii pneumonia, inflammatory cases of pneumonia such as organizing pneumonia, chronic obstructive pulmonary disease (COPD), COVID-19 pneumonia, other viral cases of pneumonia, empyema, post-obstructive pneumonia, or ventilator-associated pneumonia. **For HAP only** <u>Inclusion:</u> Adults (≥18 years) with hospital acquired pneumonia

	• 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: • 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 witnessed/known aspiration pneumonia as a result of inhaling a bolus of gastric contents.
Intervention/ Exposure/ Test	**CAP** Pitre 2023 included studies that had treatment with antibiotics and corticosteroids **HAP** Antibiotic plus corticosteroid Notes:

	• all antibiotics will be pooled • all corticosteroids will be pooled. • route of administration for antibiotic may be oral or intravenous and for corticosteroid may be oral, intravenous or by inhalation
Comparator/ Reference standard/ Confounding factors	**CAP** From Pitre 2023 SR: • standard care • placebo **HAP** Antibiotic plus placebo or antibiotic alone
Types of study to be included	Systematic reviews of RCTs and RCTs.
Other exclusion criteria	
Context	It has long been recognised that many pneumonia symptoms are caused by inflammation rather than the causative agents. Corticosteroids are a group of medications whose principal mechanism of action is through suppression of inflammation and these drugs are widely and effectively used in other non-infective disease areas. Unfortunately it is also recognised that such suppression of inflammation can increase susceptibility to infection and make on-going infections worse. For this reason there has been reluctance to use corticosteroid treatment widely in the treatment of infection. However, there is some evidence that the addition of a corticosteroid to standard antibiotic therapy at the initiation of treatment can improve outcomes for patients with pneumonia. The safety, efficacy and cost-effectiveness of this remains uncertain.

Primary outcomes (critical outcomes)	**CAP**
	From Pitre 2023:
	• mortality
	• need for invasive mechanical ventilation (in those not requiring invasive mechanical ventilation at baseline)
	• secondary infections (any type and severity
	• gastrointestinal (GI) bleeding (defined by study authors, any severity)
	• ICU admission (in those not requiring ICU admission at baseline)
	• hyperglycemia (requiring intervention)
	• duration of ICU and hospital stay.
	For all dichotomous outcomes, we collected data at the longest follow-up or closest to 90 days.
	
	HAP
	• Mortality – all cause and disease specific (at 30 days)
	• Need for invasive ventilation (in those not requiring invasive ventilation at baseline)
	• ICU / ITU admission (in those not requiring ICU/ITU admission at baseline)
	• Duration of hospital stay/duration of ICU stay
	• Clinical cure/clinical stability at the end of follow up.
	• Adverse events (at longest follow up), including:
	  ○ Gastrointestinal bleeding
	  ○ Hyperglycaemia (requiring intervention)
	  ○ Complications (composite of empyema, effusion, abscess, metastatic infection, superinfection, MODS, bacteraemia)

Secondary outcomes	• HRQoL (measured by CAP symptom questionnaire, EQ5D, or SF-36).

(important outcomes)	
Data extraction (selection and coding)	**CAP** Data from the Pitre 2023 review will be presented to the committee and will not undergo any further analysis. RoB and GRADE undertaken by the authors of that paper will be used to assess certainty of evidence. **HAP** All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. Any disagreements will be resolved by discussion with other members of the technical review team. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For SRs (including the Pitre 2023 review), 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. Minimally important differences (MIDs) will be discussed with the committee and if established MIDs are not identified, default MIDs will be used. These are 0.80 and 1.25 for dichotomous outcomes, and 0.5 times the control group SD for continuous outcomes.
Analysis of sub-groups	Analysis of subgroups will be conducted for severity status: • Low severity HAP • Moderate- and high-severity HAP The following factors will be considered for subgroup analysis if heterogeneity is present: • setting (non-hospital, hospital, ITU) • route of administration of corticosteroid • duration of corticosteroid treatment (< 7 days or ≥ 7 days) • disease aetiology • presence of relevant comorbidities (diabetes, heart disease, malignancy, chronic lung disease [including COPD], CNS disease [including dementia and

	cerebrovascular disease] renal failure, alcohol use, COPD) • dose of corticosteroid • time-to-initiation of corticosteroid • age > 75 or ≤ 75. • Viral vs bacterial pneumonia
Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)

1.4.6 Review protocol for question 6.1c: What is the clinical and cost-effectiveness of corticosteroid treatment in addition to antibiotic treatment compared with antibiotic treatment alone in babies, children and young people with CAP or HAP?

Review title	In babies, children and young people with community- or hospital-acquired pneumonia, what is the clinical and cost effectiveness of corticosteroid treatment in addition to antibiotic treatment, compared with antibiotic treatment alone?
Review question	In babies, children and young people with community- or hospital-acquired pneumonia, what is the clinical and cost effectiveness of corticosteroid treatment in addition to antibiotic treatment, compared with antibiotic treatment alone?
Objective	To understand the potential clinical and economic risks and benefits of corticosteroids as an adjunctive treatment for CAP or HAP in hospitalised babies, children and young people being treated with antibiotics.

Searches	There will be separate searches for the effectiveness and cost effectiveness evidence. **Sources for effectiveness evidence** There will be a combined search for systematic reviews covering all review questions in this guideline. This 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. The following databases will be searched for the effectiveness evidence: • 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. The following sources will be applied as required to ensure relevant records are not missed: • The reference lists of potentially relevant systematic reviews will be checked.

	• The references lists of any key potentially relevant publications will be checked where appropriate to the parameters set out in sections 6-10 below. • Later citations of any key trials or protocols identified in the search results could be checked where appropriate to the parameters set out in sections 6-10 below. • The guideline committee or other stakeholders could be asked if they are aware of any other relevant studies that could be considered. The searches for effectiveness evidence will not have any date limits applied. **Sources 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). **Managing 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. 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]). With the agreement of the guideline committee, the searches will be re-run 6-8 weeks before final submission of the review and further studies retrieved for inclusion. The information services team at NICE will quality assure the principal search strategy and peer review the other strategies. Any revisions or additional steps will be agreed by the review team before being implemented.

	The full search strategies for all databases will be published in the final review.
Condition or domain being studied	Community- or hospital-acquired pneumonia
Population	Inclusion: Babies over 28 days (corrected gestational age), children, young people (age <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). • Babies, children and young people with COVID-19 pneumonia. • Babies, children and young people who acquire pneumonia while intubated (ventilator-associated pneumonia). • Babies, children and young 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). • Babies, children and young people in whom pneumonia is an expected terminal event. • Babies, children and young people with non-pneumonic infective exacerbations of bronchiectasis. • Babies, children and young people with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • Babies, children and young people with pneumonia associated with cystic fibrosis. • Babies, children and young people with witnessed/known aspiration pneumonia as a result of inhaling a bolus of gastric contents.
Intervention/ Exposure/ Test	Antibiotic plus corticosteroid for CAP Antibiotic plus corticosteroid for HAP Notes: • all antibiotics will be pooled • all corticosteroids will be pooled. • route of administration for antibiotic may be oral or intravenous and for corticosteroid may be oral, intravenous or by inhalation
Comparator/ Reference standard/ Confounding factors	Antibiotic plus placebo or antibiotic alone
Types of study to be included	Systematic reviews of RCTs and RCTs.
Other exclusion criteria	

Context	It has long been recognised that many pneumonia symptoms are caused by inflammation rather than the causative agents. Corticosteroids are a group of medications whose principal mechanism of action is through suppression of inflammation and these drugs are widely and effectively used in other non-infective disease areas. Unfortunately it is also recognised that such suppression of inflammation can increase susceptibility to infection and make on-going infections worse. For this reason there has been reluctance to use corticosteroid treatment widely in the treatment of infection. However, there is some evidence that the addition of a corticosteroid to standard antibiotic therapy at the initiation of treatment can improve outcomes for patients with pneumonia. The safety, efficacy and cost-effectiveness of this remains uncertain.

Primary outcomes (critical outcomes)	• Mortality – all cause and disease specific (at 30 days)
	• Need for invasive ventilation (in those not requiring invasive ventilation at baseline)
	• ICU / ITU admission (in those not requiring ICU/ITU admission at baseline)
	• Duration of hospital stay, duration of ICU stay, escalation of care
	• Clinical cure/clinical stability at the end of follow up.
	• Adverse events, including:
	  ○ Gastrointestinal bleeding
	  ○ Hyperglycaemia

	○ Complications (composite of empyema, effusion, abscess, metastatic infection, superinfection, MODS, Bacteraemia) ○
Secondary outcomes (important outcomes)	• HRQoL (measured by CAP symptom questionnaire, EQ5D, or SF-36).
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. Any disagreements will be resolved by discussion with other members of the technical review team. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For SRs, the ROBIS (Risk of Bias in Systematic Reviews) checklist will be used. For RCTs, the Cochrane risk of bias (RoB) 2 tool will be used.

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. Minimally important differences (MIDs) will be discussed with the committee and if established MIDs are not identified, default MIDs will be used. These are 0.80 and 1.25 for dichotomous outcomes, and 0.5 times the control group SD for continuous outcomes.
Analysis of sub-groups	Analysis of subgroups will be conducted for severity status: • Low severity CAP • Moderate- and high-severity CAP The following factors will be considered for subgroup analysis if heterogeneity is present: • setting (hospital, ITU) • route of administration of corticosteroid • type of corticosteroid • corticosteroid dose

	• duration of treatment of steroid (< 5 days or ≥ 5 days) • disease aetiology (viral/bacterial) • dose of corticosteroid • time-to-initiation of corticosteroid • age (<2 years, 2-5, 6-12, >12)
Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)

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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 into three parts: 2A (adults with CAP), 2B (adults with HAP) and 2C (children and young people with CAP or HAP). The searches for effectiveness evidence (Part 2) were all initially run on 12 January 2024 and all had a final re-run on 21 November 2024.

- Part 3: Cost effectiveness searches

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

Search design and peer review

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

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

The MEDLINE strategies below were quality assured (QA) by a trained NICE SIS. 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) searches.

The OECD filters were applied to the main searches in January and the October 2024 reruns for Part 2. The OECD filters were removed and the whole search period was re-run on 20 November 2024 to account for any ambiguity in the review protocol.

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

Date limits

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

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

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

- Part 2A: 1 September 2022 onwards, as this was to top-up the Pitre systematic review identified in Part 1, which was last searched on 2 September 2022.

  Pitre T et al. (2023) Corticosteroids in Community-Acquired Bacterial Pneumonia: a Systematic Review, Pairwise and Dose-Response Meta-Analysis. *Journal of General Internal Medicine*, 38(11), 2593–2606.

- Part 2B: 1 March 2014 onwards as this was an update of CG191.
- Part2C: no date limit as this was a new question.

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 Part2A and Part 2C used RCT and systematic review filters. The searches for Part 2B had no filters, in case the committee wanted to review other study types, as no evidence had been found for CG191 in March 2014.

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 MEDLINE SR filter was "Health-evidence.ca Systematic review search filter" from Lee et al. (2012). The standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.

The Embase SR filter was "Health-evidence.ca Systematic review search filter" from Lee et al. (2012). The standard NICE modifications were used: pubmed.tw added to line medline.tw.

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

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 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 Part 2 were screened in three separate EPPI-R5 files. The terms for the interventions were identical in the three searches. The population terms, date limits and study filters were adjusted for each search. The table summarises the different approaches taken to the three questions:

Search approach to the effectiveness questions

Question	Condition	Population	Intervention	Limits	Date limit	Study filters	Previous work
Part 2A	CAP	Adults	Corticosteroids	Standard NICE limits	1 Sept 2022-Current	RCT or SR	SR search identified the Pitre et al. (2023) review
Part 2B	HAP	Adults	Corticosteroids	Standard NICE limits	1 March 2014-current	None	Searched in March 2014 for CG191
Part 2C	CAP or HAP	Children or young people	Corticosteroids	Standard NICE limits	None	RCT or SR	Not previously covered

As the searches for Parts 2A and 2B do not have any age-related terms, there is some overlap with the results for Part 2C. This was not problematic as the results were being screened separately.

The terms for corticosteroids were derived from checking 3 sources:

- The Stern review: Stern A et al. (2017) Corticosteroids for pneumonia. *Cochrane database of systematic reviews*, 12(12), CD007720.
- The Pitre et al. (2023) review
- The BNF - checked on 5 January 2024, last updated on 22 November 2023.

The search did not use the approach adopted in CG191, where the terms for corticosteroids were combined with those for antibiotics. It was felt that this would risk missing records that described the corticosteroid intervention as 'add-on therapy' or with 'standard therapy', or where the corticosteroid was combined with a named antibiotic.

The searches for Part 2B on hospital-acquired pneumonia (HAP) were made more specific than those used in CG191, after consultation with the technical team. This was to focus on HAP, as healthcare-associated pneumonia (HCAP) met the definition of community acquired pneumonia (CAP) used in our protocols.

The terms for children and young people in Part 2C were adopted from the standard NICE strategies used for these population groups.

The subject headings were adapted in Embase for pragmatic reasons to manage the volume of results, as direct translation had 24,618 results (compared to 6341 in MEDLINE) before applying the filters and limits. The majority of the additional volume was retrieved by exploding the terms for the drug classes steroids and corticosteroids. These were amended to be focussed and not exploded. To compensate, the Emtree terms for the drugs named in the free text were expanded. This would reduce the search to 17,467 before applying filters and limits. The free text was unchanged between MEDLINE and Embase. The search, therefore, uses more specific Emtree headings than the Stern or Pitre reviews but the risk of missing a relevant paper was minimal as it would have to be: not retrieved or unavailable

from MEDLINE or CENTRAL; not have any relevant free-text terms; and not be indexed with any of the Emtree terms still included in the search.

The main search in January 2024 applied the OECD filters in MEDLINE and Embase. The re-run searches in October 2024 for Parts 2A and 2C were limited to the first day of the month in which the main search was run to the current date using create date (.dt) and entry date (.ed) fields in MEDLINE, date created (.dc) in Embase and the post-search filter 'Date added to trials database' in CENTRAL. Part 2B was not re-run in October 2024.

The searches were then re-run again on 20 November 2024 for Parts 2A, 2B and 2C. This was to remove the OECD filters from MEDLINE and Embase. The CENTRAL searches were not altered but they were re-run to bring them up to date. In order to review any papers that had previously been removed by the OECD filter the date limits of the main search were reapplied, that is 1 September 2022 for Part 2A, 1 March 2014 for Part 2B and no date limit for Part 2C. The results from these November re-runs were added to the original EPPI-R5 files and duplicates removed in the usual way.

Part 1: Systematic review searches

Database results

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

Re-run results

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

Search strategy history

Database name: Cochrane Database of Systematic Reviews (CDSR)

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

Database name: Epistemonikos

Searches
These are the lines as they were input into the interface for the re-run:
1 title:(bronchopneumonia* OR pleuropneumonia* OR broncho-pneumonia OR pleuro-pneumonia or broncho-pneumonias OR pleuro-pneumonias OR "broncho pneumonia" OR "pleuro pneumonia" or "broncho pneumonias" OR "pleuro pneumonias")
2 abstract:(bronchopneumonia* OR pleuropneumonia* OR broncho-pneumonia OR pleuro-pneumonia or broncho-pneumonias OR pleuro-pneumonias OR "broncho pneumonia" OR "pleuro pneumonia" or "broncho pneumonias" OR "pleuro pneumonias")
3 title:(pneumonia OR pneumonias)
4 abstract:((pneumonia OR pneumonias) AND (HAP OR nosocomial* OR crossinfect* OR cross-infection OR cross-infected OR cross-infecting OR "cross infection" OR "cross infected" OR "cross infecting" or hospitalised* or hospitalized* or hospitalisation* or hospitalization*))
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))

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

Searches
(bacterial* OR chlamydial* OR mycoplasma* OR pneumococcal* OR rickettsial* OR staphylococcal* OR staphylococcus* OR necrotiz* OR necrotis* OR viral* OR organizing* OR organising* OR cryptogenic* OR bilateral* OR granulomatous* OR infectious* OR interstitial* OR neonatal* OR obstructive* OR lobar* OR escherichia* OR haemophilus* OR hemophilus* OR influenzae* OR nocardiosis* OR streptococcus* OR streptococcal*)))
Results:
Total: 48055
Apply Publication Year limits of 2014-2024: 30820
Download 1: Apply Publication type - Systematic Review: 2307
Download 2: Apply Publication type - Broad Synthesis: 223
Download 3: Apply Publication type - Structured Summary: 41
Note:
The re-run search covered the whole timespan 2014-2024 as the phrases in the free text were updated to use a version with a hyphen and to spell out the words rather than truncating them. The main search had used Publication Year limits of 2014-2023.

Part 2A: Effectiveness evidence searches (Adults with CAP)

Database results (main search)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	12/01/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 1 of 12, January 2024	71
Embase	12/01/2024	Ovid	Embase 1974 to 2024 January 11	446
MEDLINE ALL	12/01/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to January 11, 2024	129

Re-run results (October 2024)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	17/10/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 9 of 12, September 2024	33

Embase	17/10/2024	Ovid	Embase 1974 to 2024 October 16	202
MEDLINE ALL	17/10/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to October 16, 2024	73

Re-run results (November 2024)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	20/11/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 10 of 12, October 2024	113
Embase	20/11/2024	Ovid	Embase 1974 to 2024 November 19	672
MEDLINE ALL	20/11/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to November 19, 2024	195

Additional search techniques

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	11/01/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-08	21
Forward citation searching update	17/10/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-10-15	14
Reference list checking	11/01/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-08	9
Reference list checking update	17/10/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-10-15	5

Search strategy history for the main search and October 2024 re-run

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"] 5254
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 15362
#3 #1 OR #2 16983
#4 [mh Steroids] 69108
#5 steroid*:ti,ab 28649
#6 [mh "Adrenal Cortex Hormones"] 17090
#7 (Corticotherap* or ("adrenal cortex" NEXT hormone*) or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or (solu NEXT cortef*) or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or (solu NEXT medrone*) or solumedrone* or (depo NEXT medrone*) or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or (clenil NEXT modulite*) or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or (Nasobec NEXT Aqueous*) or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or (DuoResp NEXT Spiromax*) or (GoResp NEXT Digihaler*) or WockAIR* or (Wock NEXT AIR*) or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*):ti,ab 81007
#8 {or #4-#7} 139541
#9 #3 and #8 1786
#10 ((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
#11 #9 NOT #10 1313
#12 "conference":pt 233536
#13 #11 NOT #12 791
#14 #11 NOT #12 in Trials 759
Post search filter: Date added to CENTRAL trials database 01/09/2022 to 12/02/2024 71
Note in the re-run the Post search filter was changed to: Date added to CENTRAL trials database 01/01/2024 to 17/10/2024

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/ 314851
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 235716
3 1 or 2 399285
4 steroid therapy/ 36456
5 corticosteroid therapy/ 60403
6 pregnane derivative/ or exp pregnenolone derivative/ or exp hydrocortisone derivative/ or hydroxycorticosteroid/ or cortodoxone/ or exp cortisone derivative/ or exp triamcinolone derivative/ or prednisone/ or exp prednisolone derivative/ or paramethasone/ or exp dexamethasone derivative/ or clobetasol/ or beclomethasone/ or exp betamethasone derivative/ or budesonide/ or deflazacort/ or budesonide plus formoterol/ or beclomethasone dipropionate/ or tetracosactide/ or fluticasone/ or fluticasone furoate/ or azelastine plus fluticasone propionate/ or fluticasone propionate plus formoterol fumarate/ or indacaterol/ or indacaterol plus mometasone furoate/ or mometasone furoate/ or glycopyrronium bromide plus indacaterol plus mometasone furoate/ 797179
7 *corticosteroid/ or *corticosteroid derivative/ or *glucocorticoid/ or *hydroxycorticosteroid/ or *steroid/ 121227
8 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 607178
9 or/4-8 1104471
10 3 and 9 48128
11 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

Searches
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/ 1732950
12 exp "organisation for economic co-operation and development"/ or exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ or european union/ or developed country/ 3860247
13 11 not 12 1577330
14 10 not 13 46657
15 limit 14 to english language 43199
16 (letter or editorial).pt. 2095755
17 15 not 16 40836
18 Case report/ 2958814
19 17 not 18 24616
20 nonhuman/ not human/ 5363933
21 19 not 20 23508
22 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5809704
23 21 not 22 17471
24 random:.tw. 2020408
25 placebo:.mp. 531539
26 double-blind:.tw. 248382
27 or/24-26 2301141
28 23 and 27 3613
29 (MEDLINE or pubmed).tw. 427426
30 exp systematic review/ or systematic review.tw. 531767
31 meta-analysis/ 303091
32 intervention$.ti. 273771
33 or/29-32 1004723

Searches		
34	23 and 33	1167
35	28 or 34	4244
36	limit 35 to dc=20220901-20240112	446
Note: in the re-run Line 36 was changed to limit 35 to dc=20240101-20241017.		

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/ 124295
2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 160684
3	1 or 2 230532
4	exp Steroids/ 929730
5	steroid*.ti,ab. 267566
6	exp Adrenal Cortex Hormones/ 427637
7	(Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 430900
8	or/4-7 1306697
9	3 and 8 14578
10	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

Searches
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/ 1320790
11 "organisation for economic co-operation and development"/ or australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ or european union/ or developed countries/ 3541378
12 10 not 11 1230499
13 9 not 12 14088
14 limit 13 to english language 11509
15 limit 14 to (letter or historical article or comment or editorial or news or case reports) 4477
16 14 not 15 7032
17 Animals/ not (Animals/ and Humans/) 5151321
18 16 not 17 6342
19 exp Randomized Controlled Trial/ 608180
20 randomi?ed.mp. 1099019
21 placebo.mp. 252671
22 or/19-21 1165942
23 18 and 22 913
24 (MEDLINE or pubmed).tw. 344127
25 systematic review.tw. 287307
26 systematic review.pt. 249520
27 meta-analysis.pt. 193093
28 intervention$.ti. 208185
29 or/24-28 718999
30 18 and 29 409
31 23 or 30 1116
32 limit 31 to ed=20220901-20240112 97
33 limit 31 to dt=20220901-20240112 124
34 32 or 33 129
Note: in the re-run the following lines were used:
31 23 or 30
32 limit 31 to ed=20240101-20241017
33 limit 31 to dt=20240101-20241017
34 32 or 33

Search strategy history for the November 2024 re-run

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"] 4469
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 16400
#3 #1 OR #2 17658
#4 [mh Steroids] 76678
#5 steroid*:ti,ab 30032
#6 [mh "Adrenal Cortex Hormones"] 19479
#7 (Corticotherap* or ("adrenal cortex" NEXT hormone*) or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or (solu NEXT cortef*) or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or (solu NEXT medrone*) or solumedrone* or (depo NEXT medrone*) or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or (clenil NEXT modulite*) or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or (Nasobec NEXT Aqueous*) or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or (DuoResp NEXT Spiromax*) or (GoResp NEXT Digihaler*) or WockAIR* or (Wock NEXT AIR*) or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*):ti,ab 86097
#8 {or #4-#7} 149833
#9 #3 and #8 1864
#10 ((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 543957
#11 #9 NOT #10 1369
#12 "conference":pt 249832
#13 #11 NOT #12 823
#14 #11 NOT #12 in Trials 790
Post search filter: Date added to CENTRAL trials database 01/09/2022 to 20/11/2024 113

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/ 332167
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 248907
3 1 or 2 420878
4 steroid therapy/ 38148
5 corticosteroid therapy/ 63061
6 pregnane derivative/ or exp pregnenolone derivative/ or exp hydrocortisone derivative/ or hydroxycorticosteroid/ or cortodoxone/ or exp cortisone derivative/ or exp triamcinolone derivative/ or prednisone/ or exp prednisolone derivative/ or paramethasone/ or exp dexamethasone derivative/ or clobetasol/ or beclomethasone/ or exp betamethasone derivative/ or budesonide/ or deflazacort/ or budesonide plus formoterol/ or beclomethasone dipropionate/ or tetracosactide/ or fluticasone/ or fluticasone furoate/ or azelastine plus fluticasone propionate/ or fluticasone propionate plus formoterol fumarate/ or indacaterol/ or indacaterol plus mometasone furoate/ or mometasone furoate/ or glycopyrronium bromide plus indacaterol plus mometasone furoate/ 831443
7 *corticosteroid/ or *corticosteroid derivative/ or *glucocorticoid/ or *hydroxycorticosteroid/ or *steroid/ 124521
8 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 632962
9 or/4-8 1151087
10 3 and 9 51190
11 limit 10 to english language 47627
12 (letter or editorial).pt. 2179237
13 11 not 12 45083
14 Case report/ 3061599
15 13 not 14 27003
16 nonhuman/ not human/ 5568893
17 15 not 16 25807

Searches
18 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6069915
19 17 not 18 19292
20 random:.tw. 2144162
21 placebo:.mp. 549106
22 double-blind:.tw. 257672
23 or/20-22 2430610
24 19 and 23 3852
25 (MEDLINE or pubmed).tw. 473540
26 exp systematic review/ or systematic review.tw. 588896
27 meta-analysis/ 336918
28 intervention$.ti. 293772
29 or/25-28 1096065
30 19 and 29 1286
31 24 or 30 4566
32 limit 31 to dc=20220901-20241120 672

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/ 126211
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 168047
3 1 or 2 238362
4 exp Steroids/ 944169
5 steroid*.ti,ab. 276283
6 exp Adrenal Cortex Hormones/ 433540
7 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 445812
8 or/4-7 1338000
9 3 and 8 15199

Searches		
10	limit 9 to english language	12534
11	limit 10 to (letter or historical article or comment or editorial or news or case reports)	4803
12	10 not 11	7731
13	Animals/ not (Animals/ and Humans/)	5244413
14	12 not 13	7016
15	exp Randomized Controlled Trial/	628170
16	randomi?ed.mp.	1153820
17	placebo.mp.	262154
18	or/15-17	1222604
19	14 and 18	989
20	(MEDLINE or pubmed).tw.	383803
21	systematic review.tw.	324754
22	systematic review.pt.	280853
23	meta-analysis.pt.	212564
24	intervention$.ti.	224432
25	or/20-24	790351
26	14 and 25	448
27	19 or 26	1215
28	limit 27 to ed=20220901-20241120	143
29	limit 27 to dt=20220901-20241120	190
30	28 or 29	195

Additional search techniques

Forward citation searching

Date of search	11/01/24
How the seed references were identified	From the systematic review searches done for Part 1.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2015-present)
Date of last update	Data updated 2024-01-08
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.

	Removed any records published before 2022.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials.
List of seed references used	5 Systematic reviews presented to the committee on 10 Nov 2023: Bergmann F et al. (2023) Efficacy and Safety of Corticosteroid Therapy for Community-Acquired Pneumonia: A Meta-Analysis and Meta-Regression of Randomized, Controlled Trials. Clinical Infectious Diseases, 77(12), 1704–1713. Pitre T et al. (2023) Corticosteroids in Community-Acquired Bacterial Pneumonia: a Systematic Review, Pairwise and Dose-Response Meta-Analysis. Journal of General Internal Medicine, 38(11), 2593–2606. Saleem N (2022) Effect of Corticosteroids on Mortality and Clinical Cure in Community-Acquired Pneumonia: A Systematic Review, Meta-analysis, and Meta-regression of Randomized Control Trials. Chest, S0012-3692(22)03705-9. Advance online publication. Stern A et al. (2017) Corticosteroids for pneumonia. The Cochrane database of systematic reviews, 12(12), CD007720. Wu JY et al. (2023) Efficacy and safety of adjunctive corticosteroids in the treatment of severe community-acquired pneumonia: a systematic review and meta-analysis of randomized controlled trials. Critical Care, 27(1), 274. https://doi.org/10.1186/s13054-023-04561-z 18 papers included in the Pitre review: Blum CA et al. Adjunct prednisone therapy for patients with community acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2015;385(9977):1511-8. Confalonieri M et al. Hydrocortisone infusion for severe community-acquired pneumonia:

	a preliminary randomized study. Am J Respir Crit Care Med. 2005;171(3):242-8 Dequin PF et al Hydrocortisone in Severe Community-Acquired Pneumonia. N Engl J Med. 2023 May 25;388(21):1931-1941. El-Ghamrawy A, Shokeir M, Esmat A. Effects of low-dose hydrocortisone in ICU patients with severe community-acquired pneumonia. Egyptian Journal of Chest. 2006;55:91-9. Fernández-Serrano S et al. Effect of corticosteroids on the clinical course of community-acquired pneumonia: a randomized controlled trial. Critical Care. 2011;15(2):1-9. Li G, GU C, Zhang S, Lian R, Zhang G. Value of glucocorticoid steroids in the treatment of patients with severe community-acquired pneumonia complicated with septic shock. Chinese Critical Care Med. 2016:780-4. Lloyd M et al. Effectiveness of a Bundled Intervention Including Adjunctive Corticosteroids on Outcomes of Hospitalized Patients With Community-Acquired Pneumonia: A Stepped-Wedge Randomized Clinical Trial. JAMA Intern Med. 2019;179(8):1052-60. Marik P et al. Hydrocortisone and tumor necrosis factor in severe community acquired pneumonia: a randomized controlled study. Chest. 1993;104(2):389-92. McHardy VU, Schonell ME. Ampicillin dosage and use of prednisolone in treatment of pneumonia: co-operative controlled trial. Br Med J. 1972;4(5840):569-73. Meduri GU et al. Lowdose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. Intensive Care Med. 2022;48(8):1009-23. Meijvis SC et al. Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-

	blind, placebo-controlled trial. Lancet. 2011;377(9782):2023-30. Mikami K et al. Efficacy of corticosteroids in the treatment of community-acquired pneumonia requiring hospitalization. Lung.2007;185(5):249-55. Nafae RM, Ragab MI, Amany FM, Rashed SB. Adjuvant role of corticosteroids in the treatment of community-acquired pneumonia. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(3):439-45. Sabry NA, Omar EE-D. Corticosteroids and ICU course of community acquired pneumonia in Egyptian settings. Pharmacology & Pharmacy. 2011;2(02):73. Snijders D et al. Efficacy of corticosteroids in community-acquired pneumonia: a randomized double-blinded clinical trial. Am J Respir Crit Care Med.2010;181(9):975-82. Torres A et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. Jama.2015;313(7):677-86 Wagner HN et al. The effect of hydrocortisone upon the course of pneumococcal pneumonia treated with penicillin. Bull Johns Hopkins Hosp. 1956;98(3):197-215. Wittermans E et al. Adjunctive treatment with oral dexamethasone in non-ICU patients hospitalised with community-acquired pneumonia: a randomised clinical trial. Eur Respir J. 2021;58(2) Additional include from Stern review: Hatakeyama S et al. Treatment of aspiration pneumonia with low-dose methylprednisolone and antibiotics. Japanese Journal of Thoracic Diseases 1998;33(1):51-6.
No. of forward citation searching results	21

Forward citation searching update

Date of search	17/10/24
How the seed references were identified	In line with recommendation 4 of the TARCiS statement (doi:10.1136/bmj-2023-078384), that citation searching should be based on seed references meeting the inclusion criteria of the review after full-text screening of the primary search results, the included studies were identified from the draft evidence reviews presented to the committee at the same time as the database searches were re-run.
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 2024-10-15
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. Removed any records published before 2022.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials.
List of seed references used	Blum CA et al. (2023) Adjunct prednisone in community-acquired pneumonia: 180-day outcome of a multicentre, double-blind, randomized, placebo-controlled trial. BMC Pulmonary Medicine, 23(1), 500. Pitre T et al. (2023) Corticosteroids in Community-Acquired Bacterial Pneumonia: a Systematic Review, Pairwise and Dose-Response Meta-Analysis. Journal of General Internal Medicine, 38(11), 2593-2606.
No. of forward citation searching results	14

Reference list checking

Date of search	11/01/24
How the seed references were identified	From the systematic review searches done for Part 1 chose the relevant reviews published after September 2022.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-01-08
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. Removed any records published before 2022.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials.
List of seed references used	Bergmann F et al. (2023) Efficacy and Safety of Corticosteroid Therapy for Community-Acquired Pneumonia: A Meta-Analysis and Meta-Regression of Randomized, Controlled Trials. Clinical Infectious Diseases, 77(12), 1704–1713. Dequin PF et al Hydrocortisone in Severe Community-Acquired Pneumonia. N Engl J Med. 2023 May 25;388(21):1931-1941. Meduri GU et al. Lowdose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. Intensive Care Med. 2022;48(8):1009-23. Pitre T et al. (2023) Corticosteroids in Community-Acquired Bacterial Pneumonia: a Systematic Review, Pairwise and Dose-Response Meta-Analysis. Journal of General Internal Medicine, 38(11), 2593–2606.

	Saleem N (2022) Effect of Corticosteroids on Mortality and Clinical Cure in Community-Acquired Pneumonia: A Systematic Review, Meta-analysis, and Meta-regression of Randomized Control Trials. Chest, S0012-3692(22)03705-9. Advance online publication. Wu JY et al. (2023) Efficacy and safety of adjunctive corticosteroids in the treatment of severe community-acquired pneumonia: a systematic review and meta-analysis of randomized controlled trials. Critical Care, 27(1), 274.
No. of reference list checking results	9

Reference list checking update

Date of search	17/10/24
How the seed references were identified	In line with recommendation 4 of the TARCiS statement (doi:10.1136/bmj-2023-078384), that citation searching should be based on seed references meeting the inclusion criteria of the review after full-text screening of the primary search results, the included studies were identified from the draft evidence reviews presented to the committee at the same time as the database searches were re-run, noting that Pitre et al. had already been used.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-10-15
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. Removed any records published before 2022.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology.

	Did not include letters or editorials.
List of seed references used	Blum CA et al. (2023) Adjunct prednisone in community-acquired pneumonia: 180-day outcome of a multicentre, double-blind, randomized, placebo-controlled trial. BMC Pulmonary Medicine, 23(1), 500.
No. of reference list checking results	5

Part 2B: Effectiveness evidence searches (Adults with HAP)

Database results (main search)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	12/01/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 1 of 12, January 2024	31
Embase	12/01/2024	Ovid	Embase 1974 to 2024 January 11	216
MEDLINE ALL	12/01/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to January 11, 2024	131

Re-run results (November 2024)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	20/11/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 10 of 12, October 2024	34
Embase	20/11/2024	Ovid	Embase 1974 to 2024 November 19	274
MEDLINE ALL	20/11/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to November 19, 2024	160

Additional search techniques

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	11/01/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-08	0
Reference list checking	11/01/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-08	0

Search strategy history for the main search

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

Searches
#1 [mh ^"healthcare-associated pneumonia"] 47
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab and [mh ^"Cross Infection"] 382
#3 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/5 (HAP or nosocomial* or crossinfect* or (cross NEXT infect*))):ti,ab 643
#4 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/3 ((healthcare* or hospital* or (health NEXT care*) or accident* or emergenc* or ICU or (intensive NEXT care*) or (intensive NEXT treatment*) or ITU or (high NEXT dependency*) or HDU or (critical NEXT care*) or CCU or inpatient* or maternity* or clinic or clinics or ward or wards or unit or units or facility* or facilities* or "A&E" or surgery* or surgical* or (secondary NEXT care*)) NEAR/3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*))):ti,ab 689
#5 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/3 (postoperat* or perioperat* or (peri NEXT operat*) or postsurg* or posthospitali*)):ti,ab 246
#6 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/3 (after* or post* or follow* or subsequent*) NEAR/3 (hospitali* or admit* or admission* or surgery* or surgical* or operat* or transplant* or procedure* or intervention*)):ti,ab 136
#7 {or #1-#6} 1624
#8 [mh Steroids] 69108
#9 steroid*:ti,ab 28649
#10 [mh "Adrenal Cortex Hormones"] 17090
#11 (Corticotherap* or ("adrenal cortex" NEXT hormone*) or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or (solu NEXT cortef*) or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or (solu NEXT medrone*) or solumedrone* or (depo NEXT medrone*) or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or (clenil NEXT modulite*) or qvar* or becloforte* or cortisol* or tetracosactide* or

Searches
Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or (Nasobec NEXT Aqueous*) or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or (DuoResp NEXT Spiromax*) or (GoResp NEXT Digihaler*) or WockAIR* or (Wock NEXT AIR*) or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*):ti,ab 81007
#12 {or #8-#11} 139541
#13 #7 AND #12 80
#14 ((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
#15 #13 NOT #14 57
#16 "conference":pt 233536
#17 #15 NOT #16 46
#18 #15 NOT #16 in Trials 44
Post search filter: Date added to CENTRAL trials database 01/03/2014 to 12/02/2024 31

Database name: Embase

Searches
1 hospital acquired pneumonia/ 4357
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. and Cross Infection/ 1409
3 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj5 (HAP or nosocomial* or crossinfect* or "cross infect*")).ti,ab. 5774
4 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 ((healthcare* or hospital* or "health care*" or accident* or emergenc* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or CCU or inpatient* or maternity* or clinic or clinics or ward or wards or unit or units or facility* or facilities* or "A&E" or surgery* or surgical* or "secondary care*") adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*))).ti,ab. 6676
5 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (postoperat* or perioperat* or "peri operat*" or postsurg* or posthospitali*)).ti,ab. 2700
6 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (after* or post* or follow* or subsequent*) adj3 (hospitali* or admit* or admission* or surgery* or surgical* or operat* or transplant* or procedure* or intervention*)).ti,ab. 2143
7 or/1-6 17945
8 steroid therapy/ 36456
9 corticosteroid therapy/ 60403
10 pregnane derivative/ or exp pregnenolone derivative/ or exp hydrocortisone derivative/ or hydroxycorticosteroid/ or cortodoxone/ or exp cortisone derivative/ or exp triamcinolone derivative/ or prednisone/ or exp prednisolone derivative/ or paramethasone/ or exp dexamethasone derivative/ or clobetasol/ or beclomethasone/ or exp betamethasone derivative/ or budesonide/ or deflazacort/ or budesonide plus formoterol/ or beclomethasone dipropionate/ or tetracosactide/ or fluticasone/ or fluticasone furoate/ or azelastine plus fluticasone propionate/ or fluticasone propionate plus formoterol fumarate/ or indacaterol/ or

Searches
indacaterol plus mometasone furoate/ or mometasone furoate/ or glycopyrronium bromide plus indacaterol plus mometasone furoate/ 797179
11 *corticosteroid/ or *corticosteroid derivative/ or *glucocorticoid/ or *hydroxycorticosteroid/ or *steroid/ 121227
12 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 607178
13 or/8-12 1104471
14 7 and 13 1102
15 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/ 1732950
16 exp "organisation for economic co-operation and development"/ or exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or

Searches
israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ or european union/ or developed country/ 3860247
17 15 not 16 1577330
18 14 not 17 1044
19 limit 18 to english language 968
20 (letter or editorial).pt. 2095755
21 19 not 20 937
22 Case report/ 2958814
23 21 not 22 505
24 nonhuman/ not human/ 5363933
25 23 not 24 500
26 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5809704
27 25 not 26 364
28 limit 27 to dc=20140301-20240112 216

Database name: MEDLINE ALL

Searches
1 healthcare-associated pneumonia/ 351
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. and Cross Infection/ 6136
3 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj5 (HAP or nosocomial* or crossinfect* or "cross infect*")).ti,ab. 3826
4 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 ((healthcare* or hospital* or "health care*" or accident* or emergenc* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or CCU or inpatient* or maternity* or clinic or clinics or ward or wards or unit or units or facility* or facilities* or "A&E" or surgery* or surgical* or "secondary care*") adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*))).ti,ab. 4053
5 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (postoperat* or perioperat* or "peri operat*" or postsurg* or posthospitali*)).ti,ab. 1979
6 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (after* or post* or follow* or subsequent*) adj3 (hospitali* or admit* or admission* or surgery* or surgical* or operat* or transplant* or procedure* or intervention*)).ti,ab. 1353
7 or/1-6 13119
8 exp Steroids/ 929730
9 steroid*.ti,ab. 267566
10 exp Adrenal Cortex Hormones/ 427637
11 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or

Searches
deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 430900
12 or/8-11 1306697
13 7 and 12 468
14 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/ 1320790
15 "organisation for economic co-operation and development"/ or australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ or european union/ or developed countries/ 3541378
16 14 not 15 1230499
17 13 not 16 435
18 limit 17 to english language 362
19 limit 18 to (letter or historical article or comment or editorial or news or case reports) 101
20 18 not 19 261
21 Animals/ not (Animals/ and Humans/) 5151321

Searches		
22	20 not 21	257
23	limit 22 to ed=20140301-20240112	104
24	limit 22 to dt=20140301-20240112	125
25	23 or 24	131

Search strategy history for the November 2024 re-run

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

Searches	
#1	[mh ^"healthcare-associated pneumonia"] 65
#2	(pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab and [mh ^"Cross Infection"] 410
#3	((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/5 (HAP or nosocomial* or crossinfect* or (cross NEXT infect*))):ti,ab 670
#4	((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/3 ((healthcare* or hospital* or (health NEXT care*) or accident* or emergenc* or ICU or (intensive NEXT care*) or (intensive NEXT treatment*) or ITU or (high NEXT dependency*) or HDU or (critical NEXT care*) or CCU or inpatient* or maternity* or clinic or clinics or ward or wards or unit or units or facility* or facilities* or "A&E" or surgery* or surgical* or (secondary NEXT care*)) NEAR/3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*))):ti,ab 746
#5	((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/3 (postoperat* or perioperat* or (peri NEXT operat*) or postsurg* or posthospitali*)):ti,ab 275
#6	((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) NEAR/3 (after* or post* or follow* or subsequent*) NEAR/3 (hospitali* or admit* or admission* or surgery* or surgical* or operat* or transplant* or procedure* or intervention*)):ti,ab 150
#7	{or #1-#6} 1748
#8	[mh Steroids] 76678
#9	steroid*:ti,ab 30032
#10	[mh "Adrenal Cortex Hormones"] 19479
#11	(Corticotherap* or ("adrenal cortex" NEXT hormone*) or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or (solu NEXT cortef*) or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or (solu NEXT medrone*) or solumedrone* or (depo NEXT medrone*) or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or (clenil NEXT modulite*) or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or (Nasobec NEXT Aqueous*) or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or (DuoResp NEXT Spiromax*) or (GoResp NEXT Digihaler*) or WockAIR* or (Wock NEXT AIR*) or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*):ti,ab 86097
#12	{or #8-#11} 149833

Searches
#13 #7 AND #12 87
#14 ((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 543957
#15 #13 NOT #14 60
#16 "conference":pt 249832
#17 #15 NOT #16 49
#18 #15 NOT #16 in Trials 47
Post search filter: Date added to CENTRAL trials database 01/03/2014 to 20/11/2024 34

Database name: Embase

Searches
1 hospital acquired pneumonia/ 4714
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. and Cross Infection/ 1488
3 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj5 (HAP or nosocomial* or crossinfect* or "cross infect*")).ti,ab. 5979
4 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 ((healthcare* or hospital* or "health care*" or accident* or emergenc* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or CCU or inpatient* or maternity* or clinic or clinics or ward or wards or unit or units or facility* or facilities* or "A&E" or surgery* or surgical* or "secondary care*") adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*))).ti,ab. 7060
5 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (postoperat* or perioperat* or "peri operat*" or postsurg* or posthospitali*)).ti,ab. 2885
6 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (after* or post* or follow* or subsequent*) adj3 (hospitali* or admit* or admission* or surgery* or surgical* or operat* or transplant* or procedure* or intervention*)).ti,ab. 2256
7 or/1-6 18913
8 steroid therapy/ 38148
9 corticosteroid therapy/ 63061
10 pregnane derivative/ or exp pregnenolone derivative/ or exp hydrocortisone derivative/ or hydroxycorticosteroid/ or cortodoxone/ or exp cortisone derivative/ or exp triamcinolone derivative/ or prednisone/ or exp prednisolone derivative/ or paramethasone/ or exp dexamethasone derivative/ or clobetasol/ or beclomethasone/ or exp betamethasone derivative/ or budesonide/ or deflazacort/ or budesonide plus formoterol/ or beclomethasone dipropionate/ or tetracosactide/ or fluticasone/ or fluticasone furoate/ or azelastine plus fluticasone propionate/ or fluticasone propionate plus formoterol fumarate/ or indacaterol/ or indacaterol plus mometasone furoate/ or mometasone furoate/ or glycopyrronium bromide plus indacaterol plus mometasone furoate/ 831443
11 *corticosteroid/ or *corticosteroid derivative/ or *glucocorticoid/ or *hydroxycorticosteroid/ or *steroid/ 124521
12 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or

Searches
prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 632962
13 or/8-12 1151087
14 7 and 13 1176
15 limit 14 to english language 1096
16 (letter or editorial).pt. 2179237
17 15 not 16 1063
18 Case report/ 3061599
19 17 not 18 581
20 nonhuman/ not human/ 5568893
21 19 not 20 576
22 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6069915
23 21 not 22 429
24 limit 23 to dc=20140301-20241120 274

Database name: MEDLINE ALL

Searches
1 healthcare-associated pneumonia/ 391
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. and Cross Infection/ 6232
3 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj5 (HAP or nosocomial* or crossinfect* or "cross infect*")).ti,ab. 3952
4 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 ((healthcare* or hospital* or "health care*" or accident* or emergenc* or ICU or "intensive care*" or "intensive treatment*" or ITU or "high dependency*" or HDU or "critical care*" or CCU or inpatient* or maternity* or clinic or clinics or ward or wards or unit or units or facility* or facilities* or "A&E" or surgery* or surgical* or "secondary care*") adj3 (acquir* or associat* or transmission* or transmit* or onset* or contract* or catch* or caught*))).ti,ab. 4293
5 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (postoperat* or perioperat* or "peri operat*" or postsurg* or posthospitali*)).ti,ab. 2116
6 ((pneumonia or pneumonias or bronchopneumon* or pleuropneumon*) adj3 (after* or post* or follow* or subsequent*) adj3 (hospitali* or admit* or admission* or surgery* or surgical* or operat* or transplant* or procedure* or intervention*)).ti,ab. 1418
7 or/1-6 13634
8 exp Steroids/ 944169
9 steroid*.ti,ab. 276283

Searches
10 exp Adrenal Cortex Hormones/ 433540
11 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 445812
12 or/8-11 1338000
13 7 and 12 483
14 limit 13 to english language 406
15 limit 14 to (letter or historical article or comment or editorial or news or case reports) 108
16 14 not 15 298
17 Animals/ not (Animals/ and Humans/) 5244413
18 16 not 17 294
19 limit 18 to ed=20140301-20241120 131
20 limit 18 to dt=20140301-20241120 154
21 19 or 20 160

Additional search techniques

Reference list checking and forward citation searching

Date of search	11/01/24
How the seed references were identified	Reviewed the systematic review searches done for Part 1 and no relevant reviews identified on HAP. Checked the Stern Cochrane review as its scope covered HAP but it states that no relevant papers were included. Checked the relevant evidence review for CG191 and it contained no relevant papers.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present)

	• Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-01-08
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. Removed any records published before 2022.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials.
List of seed references used	None identified
No. of forward citation searching results	0
No. of reference list checking results	0

Part 2C: Effectiveness evidence searches (Children with CAP or HAP)

Database results (main search)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	12/01/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 1 of 12, January 2024	165
Embase	12/01/2024	Ovid	Embase 1974 to 2024 January 11	639
MEDLINE ALL	12/01/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to January 11, 2024	200

Re-run results (October 2024)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled	18/10/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 9 of	5

Trials (CENTRAL)			12, September 2024	
Embase	18/10/2024	Ovid	Embase 1974 to 2024 October 17	32
MEDLINE ALL	18/10/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to October 17, 2024	13

Re-run results (November 2024)

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	20/11/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 10 of 12, October 2024	175
Embase	20/11/2024	Ovid	Embase 1974 to 2024 November 19	696
MEDLINE ALL	20/11/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to November 19, 2024	222

Additional search techniques

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	11/01/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-08	19
Forward citation searching update	18/10/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-10-16	64
Reference list checking	11/01/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-01-08	28
Reference list checking update	18/10/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-10-16	62

Search strategy history for the main search and October 2024 re-run

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 15362
#3 #1 or #2 16983
#4 [mh Steroids] 69108
#5 steroid*:ti,ab 28649
#6 [mh "Adrenal Cortex Hormones"] 17090
#7 (Corticotherap* or ("adrenal cortex" NEXT hormone*) or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or (solu NEXT cortef*) or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or (solu NEXT medrone*) or solumedrone* or (depo NEXT medrone*) or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or (clenil NEXT modulite*) or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or (Nasobec NEXT Aqueous*) or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or (DuoResp NEXT Spiromax*) or (GoResp NEXT Digihaler*) or WockAIR* or (Wock NEXT AIR*) or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*):ti,ab 81007
#8 {or #4-#7} 139541
#9 #3 AND #8 1786
#10 [mh ^Infant] or [mh ^"Infant Health"] or [mh ^"Infant Welfare"] or [mh ^"Infant Care"] 29408
#11 (infan* or baby* or babies or toddler* or (pre NEXT school*) or preschool* or kindergar*):ti,ab 61115
#12 [mh Child] or [mh "Child Behavior"] or [mh ^"Child Health"] or [mh ^"Child Welfare"] or [mh ^"Child Care"] 79981
#13 [mh ^Minors] 11
#14 (child* or minor or minors or boy* or girl* or kid or kids):ti,ab 184383
#15 [mh "pediatrics"] 1180
#16 (pediatric* or paediatric*):ti,ab 41202
#17 [mh ^Adolescent] or [mh ^"Adolescent Behavior"] or [mh ^"Adolescent Health"] or [mh ^Puberty] 126411
#18 ((under NEXT 18*) or (under NEXT eighteen*)):ti,ab 16834
#19 (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 50655

#20 (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 29052
#21 {or #10-#20} 381182
#22 #9 AND #21 354
#23 ((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
#24 #22 NOT #23 214
#25 "conference":pt 233536
#26 #24 NOT #25 174
#27 #24 NOT #25 in Trials 165
Note: in the re-run an additional step was added: Post search filter: Date added to CENTRAL trials database 01/01/2024 to 18/10/2024

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/ 317699
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 235716
3 1 or 2 400438
4 steroid therapy/ 36456
5 corticosteroid therapy/ 60403
6 pregnane derivative/ or exp pregnenolone derivative/ or exp hydrocortisone derivative/ or hydroxycorticosteroid/ or cortodoxone/ or exp cortisone derivative/ or exp triamcinolone derivative/ or prednisone/ or exp prednisolone derivative/ or paramethasone/ or exp dexamethasone derivative/ or clobetasol/ or beclomethasone/ or exp betamethasone derivative/ or budesonide/ or deflazacort/ or budesonide plus formoterol/ or beclomethasone dipropionate/ or tetracosactide/ or fluticasone/ or fluticasone furoate/ or azelastine plus fluticasone propionate/ or fluticasone propionate plus formoterol fumarate/ or indacaterol/ or indacaterol plus mometasone furoate/ or mometasone furoate/ or glycopyrronium bromide plus indacaterol plus mometasone furoate/ 797179
7 *corticosteroid/ or *corticosteroid derivative/ or *glucocorticoid/ or *hydroxycorticosteroid/ or *steroid/ 121227
8 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or

Searches
beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 607178
9 or/4-8 1104471
10 3 and 9 48292
11 Juvenile/ or exp child/ or child health/ or infant welfare/ or Child Behavior/ or Child Welfare/ or exp child care/ or "minor (person)"/ 3232415
12 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 734312
13 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2646137
14 exp pediatrics/ 129160
15 (pediatric* or paediatric*).ti,ab. 725163
16 exp adolescent/ or adolescent behavior/ or adolescent health/ or exp Puberty/ 1844102
17 elementary student/ or high school student/ or middle school student/ 13290
18 ("under 18*" or "under eighteen*").ti,ab. 7729
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. 779834
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. 473642
21 or/11-20 5592945
22 10 and 21 9171
23 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

Searches
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/ 1732950
24 exp "organisation for economic co-operation and development"/ or exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ or european union/ or developed country/ 3860247
25 23 not 24 1577330
26 22 not 25 8686
27 limit 26 to english language 8135
28 (letter or editorial).pt. 2095755
29 27 not 28 7844
30 Case report/ 2958814
31 29 not 30 4339
32 nonhuman/ not human/ 5363933
33 31 not 32 4256
34 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5809704
35 33 not 34 3320
36 random:.tw. 2020408
37 placebo:.mp. 531539
38 double-blind:.tw. 248382
39 or/36-38 2301141
40 35 and 39 522
41 (MEDLINE or pubmed).tw. 427426
42 exp systematic review/ or systematic review.tw. 531767
43 meta-analysis/ 303091
44 intervention$.ti. 273771
45 or/41-44 1004723
46 35 and 45 205
47 40 or 46 639
Note: in the re-run Line 48 was added: limit 47 to dc=20240101-20241018.

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/ 124526
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 160684

Searches
3 1 or 2 230557
4 exp Steroids/ 929730
5 steroid*.ti,ab. 267566
6 exp Adrenal Cortex Hormones/ 427637
7 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 430900
8 or/4-7 1306697
9 3 and 8 14578
10 Infant/ or Infant Health/ or Infant Welfare/ or Infant Care/ 880954
11 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 616810
12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ or Child Care/ 2190563
13 Minors/ 2838
14 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2070903
15 exp pediatrics/ 63225
16 (pediatric* or paediatric*).ti,ab. 459428
17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ or Puberty/ 2236869
18 ("under 18*" or "under eighteen*").ti,ab. 4383
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. 608243
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. 345983
21 or/10-20 5001459
22 9 and 21 2768
23 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

Searches
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/ 1320790
24 "organisation for economic co-operation and development"/ or australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ or european union/ or developed countries/ 3541378
25 23 not 24 1230499
26 22 not 25 2576
27 limit 26 to english language 2086
28 limit 27 to (letter or historical article or comment or editorial or news or case reports) 719
29 27 not 28 1367
30 Animals/ not (Animals/ and Humans/) 5151321
31 29 not 30 1341
32 exp Randomized Controlled Trial/ 608180
33 randomi?ed.mp. 1099019
34 placebo.mp. 252671
35 or/32-34 1165942
36 31 and 35 162
37 (MEDLINE or pubmed).tw. 344127
38 systematic review.tw. 287307
39 systematic review.pt. 249520
40 meta-analysis.pt. 193093
41 intervention$.ti. 208185
42 or/37-41 718999
43 31 and 42 77
44 36 or 43 200
Note: in the re-run an additional step was added with Lines 45-47.
45 limit 44 to ed=20240101-20241018
46 limit 44 to dt=20240101-20241018
47 45 or 46

Search strategy history for the November 2024 re-run

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"] 4491
#2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*):ti,ab 16400
#3 #1 or #2 17660
#4 [mh Steroids] 76678
#5 steroid*:ti,ab 30032
#6 [mh "Adrenal Cortex Hormones"] 19479
#7 (Corticotherap* or ("adrenal cortex" NEXT hormone*) or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or (solu NEXT cortef*) or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or (solu NEXT medrone*) or solumedrone* or (depo NEXT medrone*) or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or (clenil NEXT modulite*) or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or (Nasobec NEXT Aqueous*) or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or (DuoResp NEXT Spiromax*) or (GoResp NEXT Digihaler*) or WockAIR* or (Wock NEXT AIR*) or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*):ti,ab 86097
#8 {or #4-#7} 149833
#9 #3 AND #8 1864
#10 [mh ^Infant] or [mh ^"Infant Health"] or [mh ^"Infant Welfare"] or [mh ^"Infant Care"] 31788
#11 (infan* or baby* or babies or toddler* or (pre NEXT school*) or preschool* or kindergar*):ti,ab 64290
#12 [mh Child] or [mh "Child Behavior"] or [mh ^"Child Health"] or [mh ^"Child Welfare"] or [mh ^"Child Care"] 84123
#13 [mh ^Minors] 15
#14 (child* or minor or minors or boy* or girl* or kid or kids):ti,ab 197561
#15 [mh "pediatrics"] 1055
#16 (pediatric* or paediatric*):ti,ab 44479
#17 [mh ^Adolescent] or [mh ^"Adolescent Behavior"] or [mh ^"Adolescent Health"] or [mh ^Puberty] 138933
#18 ((under NEXT 18*) or (under NEXT eighteen*)):ti,ab 17128
#19 (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 54512

#20 (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 31187
#21 {or #10-#20} 409633
#22 #9 AND #21 368
#23 ((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 543957
#24 #22 NOT #23 222
#25 "conference":pt 249832
#26 #24 NOT #25 185
#27 #24 NOT #25 in Trials 175

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/ 335225
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 248907
3 1 or 2 422106
4 steroid therapy/ 38148
5 corticosteroid therapy/ 63061
6 pregnane derivative/ or exp pregnenolone derivative/ or exp hydrocortisone derivative/ or hydroxycorticosteroid/ or cortodoxone/ or exp cortisone derivative/ or exp triamcinolone derivative/ or prednisone/ or exp prednisolone derivative/ or paramethasone/ or exp dexamethasone derivative/ or clobetasol/ or beclomethasone/ or exp betamethasone derivative/ or budesonide/ or deflazacort/ or budesonide plus formoterol/ or beclomethasone dipropionate/ or tetracosactide/ or fluticasone/ or fluticasone furoate/ or azelastine plus fluticasone propionate/ or fluticasone propionate plus formoterol fumarate/ or indacaterol/ or indacaterol plus mometasone furoate/ or mometasone furoate/ or glycopyrronium bromide plus indacaterol plus mometasone furoate/ 831443
7 *corticosteroid/ or *corticosteroid derivative/ or *glucocorticoid/ or *hydroxycorticosteroid/ or *steroid/ 124521
8 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or

Searches
Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 632962
9 or/4-8 1151087
10 3 and 9 51366
11 Juvenile/ or exp child/ or child health/ or infant welfare/ or Child Behavior/ or Child Welfare/ or exp child care/ or "minor (person)"/ 3364077
12 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 762936
13 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2760221
14 exp pediatrics/ 132938
15 (pediatric* or paediatric*).ti,ab. 770204
16 exp adolescent/ or adolescent behavior/ or adolescent health/ or exp Puberty/ 1927097
17 elementary student/ or high school student/ or middle school student/ 14246
18 ("under 18*" or "under eighteen*").ti,ab. 8545
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. 820547
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. 499431
21 or/11-20 5828670
22 10 and 21 9751
23 limit 22 to english language 9164
24 (letter or editorial).pt. 2179237
25 23 not 24 8848
26 Case report/ 3061599
27 25 not 26 4926
28 nonhuman/ not human/ 5568893
29 27 not 28 4839
30 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6069915
31 29 not 30 3828
32 random:.tw. 2144162
33 placebo:.mp. 549106
34 double-blind:.tw. 257672
35 or/32-34 2430610
36 31 and 35 558
37 (MEDLINE or pubmed).tw. 473540
38 exp systematic review/ or systematic review.tw. 588896
39 meta-analysis/ 336918
40 intervention$.ti. 293772
41 or/37-40 1096065
42 31 and 41 236

Searches		
43	36 or 42	696

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/ 126471
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 168047
3 1 or 2 238387
4 exp Steroids/ 944169
5 steroid*.ti,ab. 276283
6 exp Adrenal Cortex Hormones/ 433540
7 (Corticotherap* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or pregnenedione* or pregnenolone* or hydrocortisone* or hydroxypregnenolone* or hydroxycorticosteroid* or tetrahydrocortisol* or cortodoxone* or cortisone* or fludrocortisone* or corticosterone* or triamcinolone* or prednisone* or prednisolone* or paramethasone* or methylprednisolone* or dexamethasone* or clobetasol* or beclomethasone* or betamethasone* or budesonide* or efcortesol* or hydrocortone* or "solu-cortef*" or solucortef* or betnelan* or betnesol* or deflazacort* or calcort* or medrone* or "solu-medrone*" or solumedrone* or "depo-medrone*" or depomedrone* or kenalog* or novolizer* or pulmicort* or symbicort* or beclomethasone* or aerobec* or asmabec* or beclazone* or becodisks* or becotide* or "clenil modulite*" or qvar* or becloforte* or cortisol* or tetracosactide* or Glensoludex* or Dexsol* or Hydventia* or Plenadren* or Dilacort* or Kelhale* or Soprobec* or Beclu* or "Nasobec Aqueous*" or Nasacort* or Adcortyl* or Jorveza* or Cortiment* or Entocort* or Budenofalk* or Aircort* or Budeflam* or Fobumix* or "DuoResp Spiromax*" or "GoResp Digihaler*" or WockAIR* or "Wock AIR*" or Fluticasone* or Flixotide* or Flixonase* or Avamys* or Dymista* or Flutiform* or Indacaterol* or Atectura* or Mometasone* or Asmanex* or Nasonex* or Enerzair*).ti,ab. 445812
8 or/4-7 1338000
9 3 and 8 15199
10 Infant/ or Infant Health/ or Infant Welfare/ or Infant Care/ 900570
11 (infan* or baby* or babies or toddler* or "pre-school*" or preschool* or kindergar*).ti,ab. 638172
12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ or Child Care/ 2246172
13 Minors/ 2888
14 (child* or minor or minors or boy* or girl* or kid or kids).ti,ab. 2154106
15 exp pediatrics/ 64526
16 (pediatric* or paediatric*).ti,ab. 488509
17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ or Puberty/ 2293099
18 ("under 18*" or "under eighteen*").ti,ab. 4894
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. 640318
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. 364275

Searches		
21	or/10-20	5162307
22	9 and 21	2856
23	limit 22 to english language	2337
24	limit 23 to (letter or historical article or comment or editorial or news or case reports)	776
25	23 not 24	1561
26	Animals/ not (Animals/ and Humans/)	5244413
27	25 not 26	1535
28	exp Randomized Controlled Trial/	628170
29	randomi?ed.mp.	1153820
30	placebo.mp.	262154
31	or/28-30	1222604
32	27 and 31	180
33	(MEDLINE or pubmed).tw.	383803
34	systematic review.tw.	324754
35	systematic review.pt.	280853
36	meta-analysis.pt.	212564
37	intervention$.ti.	224432
38	or/33-37	790351
39	27 and 38	85
40	32 or 39	222

Additional search techniques

Forward citation searching

Date of search	11/01/24
How the seed references were identified	From the systematic review searches done for Part 1 chose any relevant reviews specifically about children. Checked the Stern Cochrane review and it states 4 of the included papers were about children.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-01-08
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. Removed any records published before 2022.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials. Excluded papers specifying adults (included those mentioning children or with no age group in the title).
List of seed references used	Luo Z, Luo J, Liu E, Xu X, Liu Y, Zeng F, et al. Effects of prednisolone on refractory Mycoplasma pneumoniae pneumonia in children. Pediatric Pulmonology 2014;49(4):377-80. Nagy B, Gaspar I, Papp A, Bene Z, Nagy B, Voko Z, et al. Efficacy of methylprednisolone in children with severe community acquired pneumonia. Pediatric Pulmonology 2013;48(2):168-75. Qiu J.-L et al. (2020) Efficacy and safety of azithromycin combined with glucocorticoid on refractory Mycoplasma pneumoniae pneumonia in children: A PRISMA-compliant systematic review and meta-Analysis. Medicine (United States), 99(22), E20121. Stern A et al. (2017) Corticosteroids for pneumonia. The Cochrane database of systematic reviews, 12(12), CD007720. Van Woensel JB, Vyas H, STAR Trial Group. Dexamethasone in children mechanically ventilated for lower respiratory tract infection caused by respiratory syncytial virus: a randomized controlled trial. Critical Care Medicine 2011;39(7):1779-83. Wu YJ, Sun J, Zhang JH, Feng LL. Clinical efficacy of adjuvant therapy with glucocorticoids in children with lobar pneumonia caused by Mycoplasma pneumoniae . Zhongguo Dang Dai Er Ke Za Zhi [Chinese Journal of Contemporary Pediatrics] 2014;16(4):401-5.
No. of forward citation searching results	19

Forward citation searching update

Date of search	18/10/24
How the seed references were identified	In line with recommendation 4 of the TARCiS statement (doi:10.1136/bmj-2023-078384), that citation searching should be based on seed references meeting the inclusion criteria of the review after full-text screening of the primary search results, the included studies were identified from the draft evidence reviews presented to the committee at the same time as the database searches were re-run. There were 5 included studies and Nagy et al. was included again in case it had been cited since the main search was done in January 2024. Also added the Kohns Vasconcelos study as it had been flagged as the protocol for an RCT that should have been completed since the main search (expected completion date at NCT03474991 is March 2024).
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-10-16
How results were managed	Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials. Excluded papers specifying adults (included those mentioning children or with no age group in the title).
List of seed references used	Kohns Vasconcelos M et al. (2020) Randomised placebo-controlled multicentre effectiveness trial of adjunct betamethasone therapy in hospitalised children with community-acquired pneumonia: a trial protocol for the KIDS-STEP trial. BMJ Open, 10(12).

	Kun J et al. (2018) Effect of combination of methylprednisolone and azithromycin on pediatric mycoplasma pneumonia and its effects on procalcitonin, hs-crp, cardiac troponin and il-2. Acta Medica Mediterranea, 34(3), 805-809. Nagy B et al. (2013) Efficacy of methylprednisolone in children with severe community acquired pneumonia. Pediatric Pulmonology, 48(2): 168-75. Shan L-S et al. (2017) Effects of methylprednisolone or immunoglobulin when added to standard treatment with intravenous azithromycin for refractory Mycoplasma pneumoniae pneumonia in children. World Journal of Pediatrics, 13(4), 321-327. Wang J & Zhang Y (2022) The effect of methylprednisolone combined with macrolide antibiotics on mycoplasma pneumoniae pneumonia in children. Farmacia, 70(5), 850-854. Tagarro A et al. (2017) Dexamethasone for Parapneumonic Pleural Effusion: A Randomized, Double-Blind, Clinical Trial. Journal of Pediatrics, 185, 117-123e6.
No. of forward citation searching results	64

Reference list checking

Date of search	11/01/24
How the seed references were identified	From the systematic review searches done for Part 1 chose any relevant reviews specifically about children. Checked the Stern Cochrane review and it states 4 of the included papers were about children.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)

Date of last update	Data updated 2024-01-08
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. Removed any records published before 2022.
How the results were selected	Included any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials. Excluded papers specifying adults (included those mentioning children or with no age group in the title).
List of seed references used	Luo Z, Luo J, Liu E, Xu X, Liu Y, Zeng F, et al. Effects of prednisolone on refractory Mycoplasma pneumoniae pneumonia in children. Pediatric Pulmonology 2014;49(4):377-80. Nagy B, Gaspar I, Papp A, Bene Z, Nagy B, Voko Z, et al. Efficacy of methylprednisolone in children with severe community acquired pneumonia. Pediatric Pulmonology 2013;48(2):168-75. Qiu J.-L et al. (2020) Efficacy and safety of azithromycin combined with glucocorticoid on refractory Mycoplasma pneumoniae pneumonia in children: A PRISMA-compliant systematic review and meta-Analysis. Medicine (United States), 99(22), E20121. Stern A et al. (2017) Corticosteroids for pneumonia. The Cochrane database of systematic reviews, 12(12), CD007720. Van Woensel JB, Vyas H, STAR Trial Group. Dexamethasone in children mechanically ventilated for lower respiratory tract infection caused by respiratory syncytial virus: a randomized controlled trial. Critical Care Medicine 2011;39(7):1779-83. Wu YJ, Sun J, Zhang JH, Feng LL. Clinical efficacy of adjuvant therapy with glucocorticoids in children with lobar pneumonia caused by Mycoplasma pneumoniae . Zhongguo Dang Dai Er Ke Za Zhi [Chinese Journal of Contemporary Pediatrics] 2014;16(4):401-5.

No. of reference list checking results	28

Reference list checking update

Date of search	18/10/24
How the seed references were identified	In line with recommendation 4 of the TARCiS statement (doi:10.1136/bmj-2023-078384), that citation searching should be based on seed references meeting the inclusion criteria of the review after full-text screening of the primary search results, the included studies were identified from the draft evidence reviews presented to the committee at the same time as the database searches were re-run. There were 5 included studies and Nagy et al. was not included as its references had been checked during the main search in January 2024.
Databases used	Web of Science (WOS) Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2019-present)
Date of last update	Data updated 2024-10-15
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 any papers on steroids for pneumonia. Did not include COVID-19, methods or epidemiology. Did not include letters or editorials. Excluded papers specifying adults (included those mentioning children or with no age group in the title).
List of seed references used	Kohns Vasconcelos M et al. (2020) Randomised placebo-controlled multicentre effectiveness trial of adjunct betamethasone therapy in hospitalised children with community-acquired pneumonia: a trial protocol for the KIDS-STEP trial. BMJ Open, 10(12). Kun J et al. (2018) Effect of combination of methylprednisolone and azithromycin on pediatric mycoplasma pneumonia and its

	effects on procalcitonin, hs-crp, cardiac troponin and il-2. Acta Medica Mediterranea, 34(3), 805-809. Nagy B et al. (2013) Efficacy of methylprednisolone in children with severe community acquired pneumonia. Pediatric Pulmonology, 48(2): 168-75. Shan L-S et al. (2017) Effects of methylprednisolone or immunoglobulin when added to standard treatment with intravenous azithromycin for refractory Mycoplasma pneumoniae pneumonia in children. World Journal of Pediatrics, 13(4), 321-327. Wang J & Zhang Y (2022) The effect of methylprednisolone combined with macrolide antibiotics on mycoplasma pneumoniae pneumonia in children. Farmacia, 70(5), 850-854. Tagarro A et al. (2017) Dexamethasone for Parapneumonic Pleural Effusion: A Randomized, Double-Blind, Clinical Trial. Journal of Pediatrics, 185, 117-123e6.
No. of reference list checking results	62

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

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
NHS Economic Evaluation Database (NHS EED)	20/11/2023	CRD	Archived – last updated 31 March 2015	11

Re-run results

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

Search strategy history

Database name: Econlit

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

Searches
4 cost utility analysis/ 12471
5 quality adjusted life year/ 35716
6 cost*.ti. 195365
7 (cost* adj2 utilit*).tw. 12784
8 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw.385741
9 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 66452
10 (qualit* adj2 adjust* adj2 life*).tw. 27335
11 QALY*.tw. 26801
12 (incremental* adj2 cost*).tw. 28720
13 ICER.tw. 13032
14 utilities.tw. 15135
15 markov*.tw. 40152
16 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw.72706
17 ((utility or effective*) adj2 analys*).tw. 37800
18 (willing* adj2 pay*).tw. 14735
19 (EQ5D* or EQ-5D*).tw. 26137
20 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 5262
21 (european* adj2 quality adj3 ("5" or five)).tw. 996
22 or/4-21 635358
23 3 and 22 7788
24 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic 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

Searches
vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ 1716014
25 exp "organisation for economic co-operation and development"/ 2774
26 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ 3801223
27 european union/ 31487
28 developed country/ 35727
29 or/25-28 3834983
30 24 not 29 1561961
31 23 not 30 6971
32 limit 31 to english language 6647
33 (letter or editorial).pt. 2081948
34 32 not 33 6549
35 Case report/ 2939178
36 34 not 35 6182
37 nonhuman/ not human/ 5325269
38 36 not 37 6027
39 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5742113
40 38 not 39 4181
41 limit 40 to yr="2014 -Current" 2288
Note: in the re-run Line 41 was changed to limit 40 to dc=20231101-20241014.

Database name: International HTA Database (INAHTA)

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

Database name: MEDLINE ALL

Searches
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, rickettsial/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or cryptogenic organizing pneumonia/ or healthcare-associated pneumonia/ 125178
2 (pneumonia or pneumonias or bronchopneumon* or pleuropneumon*).ti,ab. 159311
3 1 or 2 229286
4 Cost-Benefit Analysis/ 93463
5 Quality-Adjusted Life Years/ 15940
6 Markov Chains/ 16047
7 exp Models, Economic/ 16244
8 cost*.ti. 146284
9 (cost* adj2 utilit*).tw. 7812
10 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw.279720
11 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 47585
12 (qualit* adj2 adjust* adj2 life*).tw. 18059
13 QALY*.tw. 14611
14 (incremental* adj2 cost*).tw. 17628
15 ICER.tw. 6134
16 utilities.tw. 9537
17 markov*.tw. 32169
18 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw.54722
19 ((utility or effective*) adj2 analys*).tw. 25292
20 (willing* adj2 pay*).tw. 9954
21 (EQ5D* or EQ-5D*).tw. 13646
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/

Searches
or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ 1312779
27 "organisation for economic co-operation and development"/ 565
28 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ 3515662
29 european union/ 17814
30 developed countries/ 21444
31 or/27-30 3531767
32 26 not 31 1222696
33 25 not 32 3418
34 limit 33 to english language 3185
35 limit 34 to (letter or historical article or comment or editorial or news or case reports) 181
36 34 not 35 3004
37 Animals/ not (Animals/ and Humans/) 5137547
38 36 not 37 2921
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

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

Appendix C – Effectiveness evidence study selection

Figure 1: Study selection for RQ6.1a Community-acquired pneumonia in adults

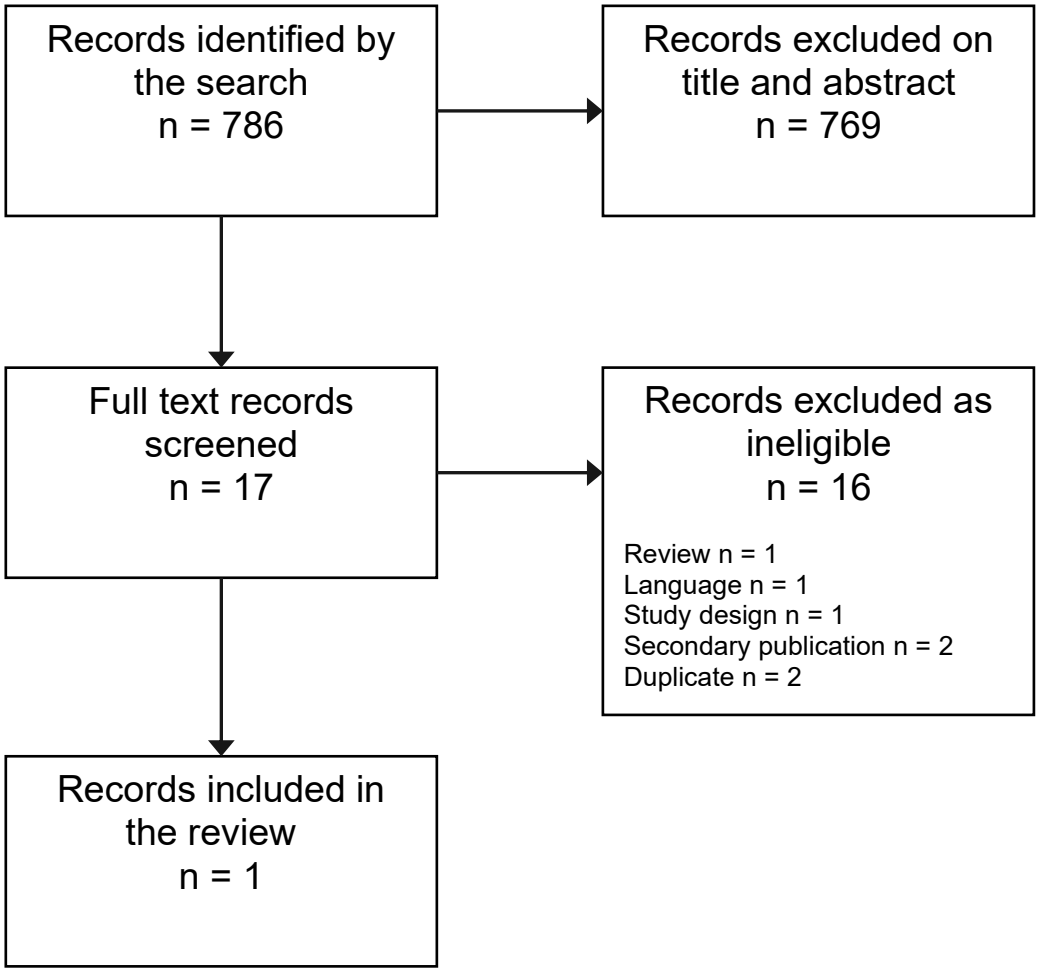


Figure 2: Study selection for RQ6.1b Hospital-acquired pneumonia in adults

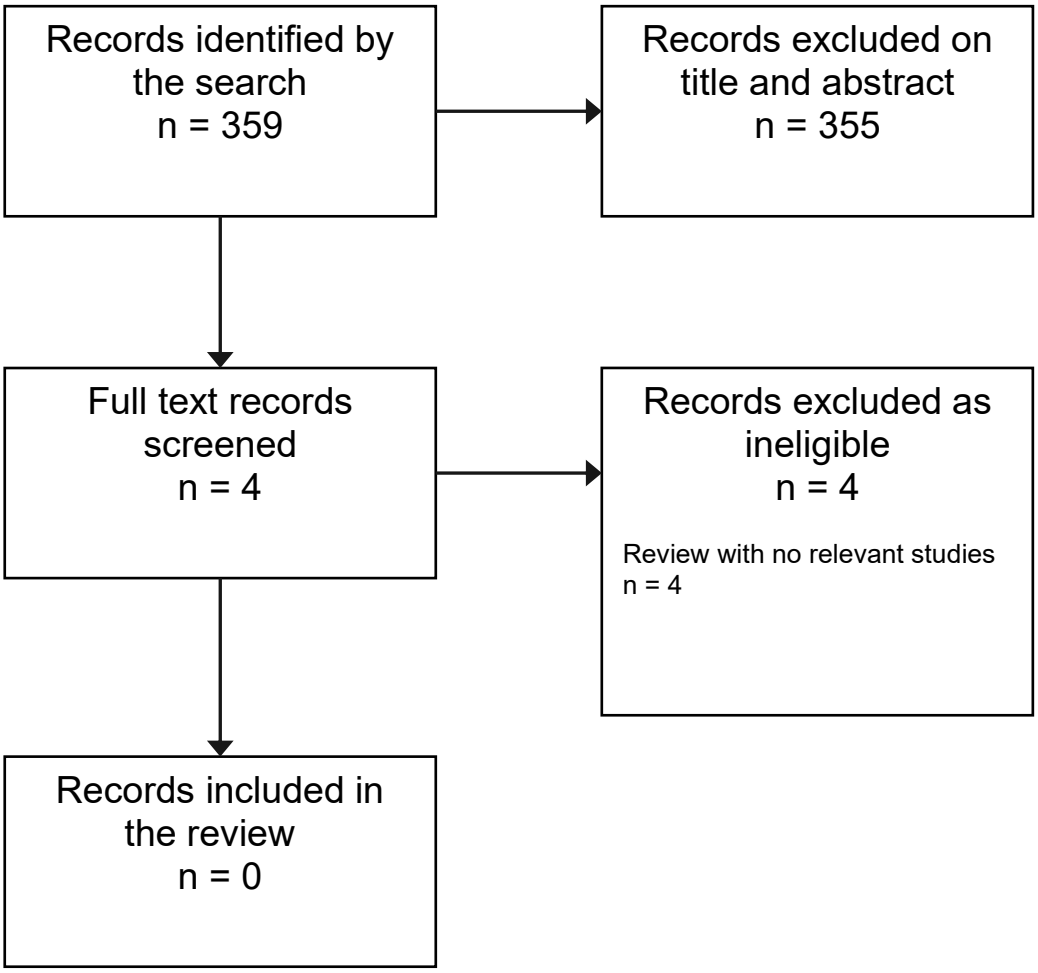
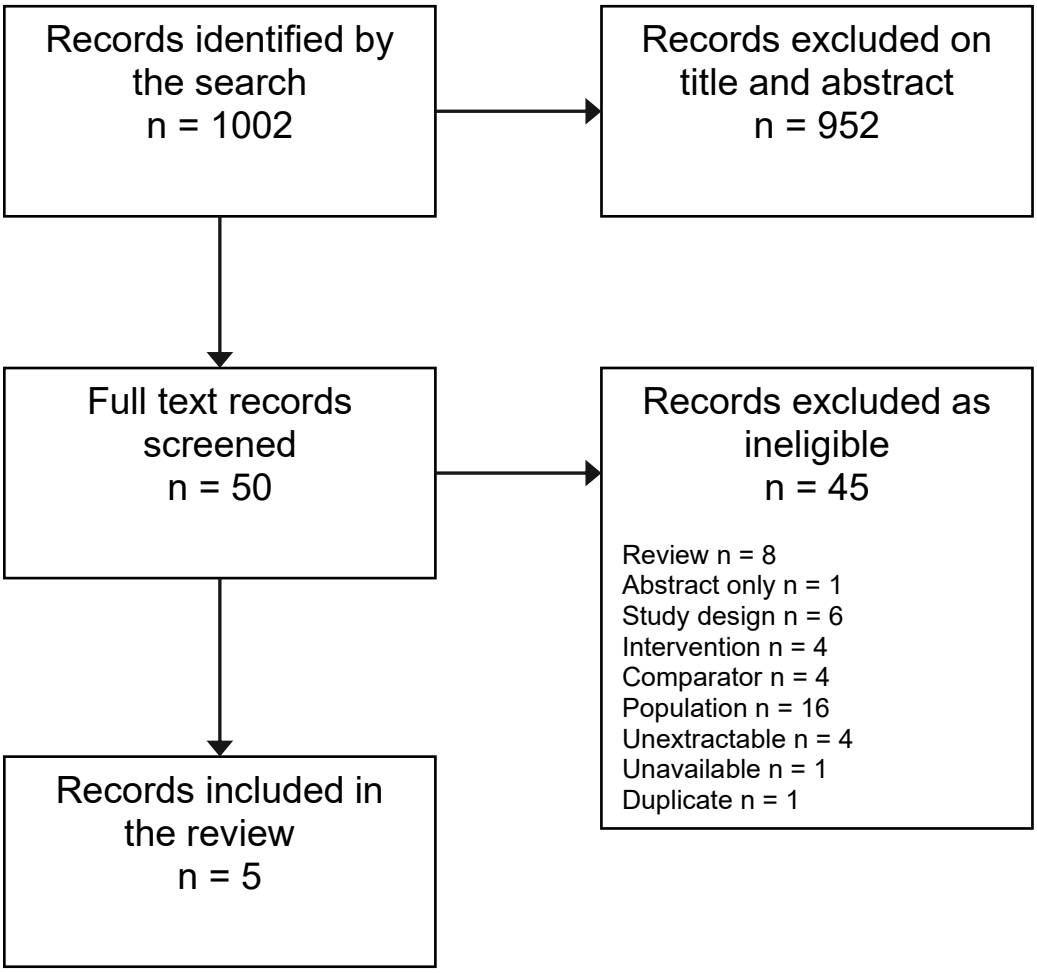


Figure 3: Study selection for RQ6.1c CAP and HAP in babies, children, and young people



Appendix D – Effectiveness evidence

Adults

Pitre, 2023

Bibliographic Reference	Pitre, Tyler; Abdali, Daniyal; Chaudhuri, Dipayan; Pastores, Stephen M; Nei, Andrea M; Annane, Djillali; Rochwerg, Bram; Zeraatkar, Dena; Corticosteroids in Community-Acquired Bacterial Pneumonia: a Systematic Review, Pairwise and Dose-Response Meta-Analysis.; Journal of general internal medicine; 2023; vol. 38 (no. 11); 2593-2606

Study Characteristics

Study design	Systematic review
Study details	Dates searched The search strategy was based on the last major review which was first published in 2015, then updated in February 2020. Updated from February 29, 2020, to September 5, 2022. Databases searched Embase, Medline, Cochrane Central Register of Controlled Trials (CENTRAL), and clinicaltrials Sources of funding No information provided
Inclusion criteria	adult patients (≥18 years old) hospitalized with probable or suspected CAP all severities of disease
Exclusion criteria	predominately (≥80%) patients with Pneumocystis jirovecii pneumonia, inflammatory cases of pneumonia such as organizing pneumonia, chronic obstructive pulmonary disease (COPD), COVID-19 pneumonia, other viral cases of pneumonia, empyema, post-obstructive pneumonia, or ventilator-associated pneumonia
Intervention(s)	treatment with corticosteroids + antibiotics usual care
Outcome(s)	Mortality Invasive Mechanical Ventilation Need for ICU Admission

	Duration of Hospitalization Duration of ICU stay Adverse Events: Secondary Infections, Gastrointestinal Bleeding, and Hyperglycaemia Ventilator-free days
Number of studies included in the systematic review	18
Studies from the systematic review that are relevant for use in the current review	Blum (2015) Confalonieri (2005) Dequin (2023) (CAPE COD) El-Ghamrawy (2006) Fernandez-Serrano (2011) Li (2016) (Cited as Gang (2016) Lloyd (2019) (IMPROVe-GAP) Marik (1993) McHardy and Schonell (1972) Meduri (2022) (ESCAPe) Meijvis (2011) (Ovidius) Mikami (2007) Nafae (2013) Sabry (2011) Snijders (2010) Torres (2015) Wagner (1956) Wittermans (2021)

Studies from the systematic review that are not relevant for use in the current review	None

CAP= community acquired pneumonia; COPD= chronic obstructive pulmonary disease; ICU= intensive care unit

Critical appraisal - ROBIS checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	High *(Risk of inaccurate findings due to multiple errors in transcription of data from primary studies and missing detail on outcomes and control conditions)*
Overall study ratings	Applicability as a source of data	Fully applicable

Blum, 2023

Bibliographic Reference	Blum, Claudine A; Roethlisberger, Eva A; Cesana-Nigro, Nicole; Winzeler, Bettina; Rodondi, Nicolas; Blum, Manuel R; Briel, Matthias; Mueller, Beat; Christ-Crain, Mirjam; Schuetz, Philipp; Adjunct prednisone in community-acquired pneumonia: 180-day outcome of a multicentre, double-blind, randomized, placebo-controlled trial.; BMC pulmonary medicine; 2023; vol. 23 (no. 1); 500

Study details

Secondary publication of another included study- see primary study for details	Secondary publication of Blum 2015 which was included in the meta-analysis by Pitre 2023
Trial registration number and/or trial name	NCT00973154
Study type	Randomised controlled trial (RCT)
Study location	Switzerland
Study setting	tertiary care hospitals
Study dates	Dec 1, 2009, to May 21, 2014
Sources of funding	University Hospital, Basel, Switzerland
Inclusion criteria	Patients 18 years of age or older admitted for hospitalization from the community or a nursing home with CAP.
Exclusion criteria	Patients or family members unable to give written informed consent, e.g. with severe dementia. Patients with active intravenous drug use. Severe immunosuppression; patients with cystic fibrosis as well as patients with active tuberculosis. Patients with acute burn injury Patients with acute gastrointestinal bleeding within 3 months of the current hospitalization Patients with an acute concomitant condition requiring more than 0.5mg/kg/d prednisone equivalent Pregnancy or breast feeding Patients with known adrenal insufficiency
Intervention(s)	50mg per day of prednisone orally for 7 days + antibiotics

Comparator	Placebo + antibiotics
Outcome measures	Mortality Secondary infections
Number of participants	802 eligible patients were enrolled in the original trial and randomly assigned to receive either prednisone or placebo. After blinded post-randomisation exclusion of 18 patients not meeting eligibility criteria, 392 patients were allocated to the prednisone group and 392 patients to the placebo group. The intention-to-treat analysis further excluded 57 patients. Therefore, 361 patients were available for the intention-to-treat analysis at 180 days in the prednisone arm and 366 patients in the placebo arm.
Duration of follow-up	180 days
Loss to follow-up	Loss since 30 day follow up: Prednisone = 7, placebo = 2.
Methods of analysis	For the primary endpoint, an adjusted hazard ratio (HR) and 95% CI was calculated using Cox proportional hazards regression based on the binary outcome of survival or death from any cause. Secondary endpoints were calculated by logistic regression based on the binary outcome of occurrence of particular adverse event or no occurrence.
Additional comments	Data extracted for outcomes used in the previous analysis by Pitre (2023)

CAP= community acquired pneumonia

Study arms

Prednisone (N = 361)
Treatment with Prednisone corticosteroid

Placebo (N = 366)
Usual care with placebo

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 *(Methodological RoB given by Pitre (2023) for the STEP trial overall. Outcome RoB assessed by NICE for Blum (2023) findings.)*
Overall bias and Directness	Overall Directness	Directly applicable

Babies, children, and young people

Kun, 2018

Bibliographic Reference	Kun, J.; Chao, W.; Silei, Y.; Effect of combination of methylprednisolone and azithromycin on pediatric mycoplasma pneumonia and its effects on procalcitonin, hs-crp, cardiac troponin and il-2; Acta Medica Mediterranea; 2018; vol. 34 (no. 3); 805-809

Study details

Study type	Randomised controlled trial (RCT)
Trial registration number and/or trial name	NR
Study location	China
Study setting	Shanghai Children's Hospital - Department of respiratory medicine, Affiliated Children's Hospital of Shanghai Jiao Tong University
Study dates	March 2014 to March 2017
Sources of funding	NR
Inclusion criteria	Positive serum mycoplasma antigen Positive cold agglutination detection Clinical symptoms and chest X-ray consistent with the clinical diagnosis of children with paediatric mycoplasma pneumonia. All patients were informed and agreed to participate in the study
Exclusion criteria	Exclusion criteria The exclusion criteria were: immunodeficiency; allergy to methylprednisolone or azithromycin; presence of organ disease (heart, lung, liver, kidney or any other vital organs), and mental disorders.
Intervention(s)	In addition to antibiotics, the observation group was given methylprednisolone intravenously at a dose of 1 mg / kg daily. When their body temperature normalized, they were given oral methylprednisolone at a dose of 1 mg / kg orally daily.
Comparator	In the control group, azithromycin was intravenously given through drip at a dose of 10 mg / kg daily. When the body temperature normalized, each patient was given oral azithromycin (10 mg / kg daily).
Outcome measures	Length of hospital stay Adverse events Clinical cure/efficiency
Number of participants	100

Duration of follow-up	The two groups of patients were treated for 4 days, then stopped 3d, this is a course of treatment, a total of 3 courses of treatment were conducted. Two groups of patients in the treatment of a course were evaluated for clinical treatment
Loss to follow-up	0
Methods of analysis	Data were analysed using SPSS18.0. Measurement data are expressed as mean ± standard deviation, and analysed using Student's t-test
Additional comments	All patients were treated with conventional therapy including antipyretic, anti-asthma, and expectorant

NR= not reported

Study arms

Intervention group (N = 50)

Methylprednisolone combined with azithromycin

Control group (N = 50)

azithromycin alone

Characteristics

Arm-level characteristics

Characteristic	Intervention group (N = 50)	Control group (N = 50)
Mean age (SD) Mean (SD)	6.6 (0.9)	6.8 (1.1)
No. of males Sample size	n = 23 ; % = 46	n = 23 ; % = 46
Duration of illness (days) Mean (SD)	3.5 (0.5)	3.7 (0.6)

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	Moderate *(Lack of information on methods process)*
Overall bias and Directness	Overall Directness	Directly applicable

Nagy, 2013

Bibliographic Reference	Nagy, Bela; Gaspar, Imre; Papp, Agnes; Bene, Zsolt; Nagy, Bela Jr; Voko, Zoltan; Balla, Gyorgy; Efficacy of methylprednisolone in children

with severe community acquired pneumonia.; Pediatric pulmonology; 2013; vol. 48 (no. 2); 168-75

Study details

Trial registration number and/or trial name	The National Ethics Committee for Clinical Pharmacology, Medical Research Council, Budapest, Hungary approved the trial (EudraCT registration number: 2007-006602-24.).
Study type	Randomised controlled trial (RCT)
Study location	Hungary
Study dates	Patients were enrolled from June 2007 through September 2009
Sources of funding	NR
Inclusion criteria	Less than 18 years of age, pallor or cyanosis, irritability or lethargy, cough, axillary body temperature (>38.58C), symptoms of respiratory distress (dyspnoe, respiratory rate: >2SD above normal value for age), new consolidation on chest X-ray, and positive laboratory tests for systemic inflammatory response syndrome (SIRS) such as elevated white blood cell (WBC) counts with >10% immature neutrophils, $P_aO_2 \geq 92$ Hgmm, tachycardia (>2SD above normal value for age), increased blood pressure (systolic value >90 Hgmm and diastolic value >60 Hgmm, i.e., no sepsis-induced hypotension)
Exclusion criteria	Chronic respiratory disease, asthma, other severe systemic disease, malignancy, previous adverse reaction to corticosteroids, or known immunodeficiency.
Intervention(s)	59 patients with severe CAP were eligible and randomized. 29 children were randomly assigned to receive i.v. methylprednisolone 20 mg (0.5–2.0 mg/kg body weight in different ages) in addition to antibiotics (imipenem 60 mg/body weight kg)
Comparator	30 children were randomly assigned to receive 5% dextrose as placebo in addition to antibiotics (imipenem 60 mg/body weight kg)
Outcome measures	Length of hospital stay Adverse events
Number of participants	59 patients were eligible to be randomised
Loss to follow-up	0 - all subjects randomised were included in the analysis
Methods of analysis	Normally distributed variables were analysed by using two-tailed Student's independent t-test. Nonparametric parameters between the two distinct treatment groups were compared by using Mann–Whitney U-test or chi-

	square test as appropriate. The significance of differences in the length of hospital stay was tested by analysis of variance (ANOVA) using the Bonferroni correction for multiple comparisons.
Additional comments	NR

NR= not reported; CAP= community acquired pneumonia; IV= intravenous;

Study arms

Intervention group (N = 29)

5-day adjuvant methylprednisolone therapy to imipenem in 29 children with severe CAP

Control group (N = 30)

30 subjects with the same disease were treated with imipenem and placebo

Characteristics

Arm-level characteristics

Characteristic	Intervention group (N = 29)	Control group (N = 30)
Mean age (SD) Mean (SD)	4.6 (2.7)	5.2 (4)
No. of females No of events	n = 13 ; % = 45	n = 11 ; % = 37

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	Moderate (Unblinded study)
Overall bias and Directness	Overall Directness	Directly applicable

Shan, 2017

Bibliographic Reference	Shan, L.-S.; Liu, X.; Kang, X.-Y.; Wang, F.; Han, X.-H.; Shang, Y.-X.; Effects of methylprednisolone or immunoglobulin when added to standard treatment with intravenous azithromycin for refractory Mycoplasma pneumoniae pneumonia in children; World Journal of Pediatrics; 2017; vol. 13 (no. 4); 321-327

Study details

Trial registration number and/or trial name	NR

Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	Children hospitalized in the Pediatric Pulmonology Department, Shengjing Hospital of China Medical University,
Study dates	The study was performed between May 2013 and May 2015
Sources of funding	This study was funded by Natural Science Foundation of Liaoning Province of China
Inclusion criteria	Age ≥2 years and <14 years CAP diagnosed by clinical manifestation, physical examination and radiology The infection was determined by the serological test using MP immunoassay enzyme-linked immunosorbent assay kits and polymerase chain reaction test of nasopharyngeal swabs.
Exclusion criteria	Children who have a history of tuberculosis, bronchiectasis, lung tumour, or nosocomial pneumonia Obvious malnutrition, unconsciousness, chronic pulmonary and cardiac disease, congenital disease, immunodeficiency Mechanical ventilation indication Discharge within 8 hours after enrolment Other pathogens were found Children younger than 2 years were all excluded because of a high rate of respiratory viral infections.
Intervention(s)	In the first three days, group A (n=56) received the additional intravenous methylprednisolone (2 mg/kg/day, 3 days); group B (n=56) received IV azithromycin 400 mg/kg/day, for 3 days, in addition to antibiotics.* *Group B did not meet inclusion criteria for this review; therefore this data was not included in the analysis.
Comparator	Group C (n=56) received IV azithromycin alone without additional therapy. Data was collected after 7 days. Further treatments were given after 7 days and data collected at follow up after 2 weeks, however only data from the first collection (after 7 days) was included in this analysis. All groups received water-electrolyte balance maintenance, sputum aspiration and other comprehensive treatments.
Outcome measures	Pleural infusion disappearance rate % C-reactive protein (mg/l)
Number of participants	A total of 168 patients were included in this study.

Duration of follow-up	All patients were followed for 7 days
Loss to follow-up	In total, 17 (10.1%) patients were considered drop-outs [4 (7.1%) in group A, 7 (12.5%) in group B and 6 (10.7%) in group C, P>0.1]. The reasons for drop-outs were as follows: withdrawal of consent, antibiotic stop within 48 hours, non-compliance, and loss of follow-up. Therefore, data of 151/168 children were available: 52/151 in group A, 49/151 in group B and 50/151 in group C
Methods of analysis	All of the data were analysed using SPSS 13.0. Chi squared test, to compare categorical variables and one-way analysis of variance (ANOVA) was used to compare continuous variables. The mean±standard deviation expresses the central tendency of the data. P<0.05 was considered statistically significant.
Additional comments	Refractory pneumonia was defined as follows: 1) fever for 7 days or more (from start of appropriate antibiotic treatment) or 2) persistent consolidation of more than one lobe of the lung despite appropriate antibiotic treatment, including macrolides. All patients required the administration of intravenous macrolide antibiotics according to the Infectious Diseases Society of America guidelines.

NR= not reported; CAP= community acquired pneumonia; MP= mycoplasma pneumonia; IV= intravenous

Study arms

Group A (N = 52)
group A [intravenous azithromycin (IA)+ methylprednisolone]

Group B (N = 49)
IA plus intravenous immunoglobulin (IVIG)

Group C (N = 25)
IA alone

Characteristics

Arm-level characteristics

Characteristic	Group A (N = 52)	Group B (N = 49)	Group C (N = 25)
Mean age (SD) Mean (SD)	7.36 (2.33)	7.36 (2.32)	7.29 (3.03)
No. of males No of events	n = 26 ; % = 50	n = 25 ; % = 51	n = 26 ; % = 52

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 *(A major limitation of this trial is its "open" design. Because there is no placebo control group, a placebo effect cannot be excluded)*
Overall bias and Directness	Overall Directness	Directly applicable

Tagarro, 2017

Bibliographic Reference Tagarro, Alfredo; Otheo, Enrique; Baquero-Artigao, Fernando; Navarro, Maria-Luisa; Velasco, Rosa; Ruiz, Marta; Penin, Maria; Moreno, David; Rojo, Pablo; Madero, Rosario; Dexamethasone for Parapneumonic Pleural Effusion: A Randomized, Double-Blind, Clinical Trial.; The Journal of pediatrics; 2017; vol. 185; 117-123e6

Study details

Trial registration number and/or trial name	NR
Study type	Randomised controlled trial (RCT)
Study location	Spain
Study setting	Tertiary care, teaching hospitals
Study dates	NR
Sources of funding	NR
Inclusion criteria	Inclusion criteria Children (1 mo-14 y) admitted for pneumonia (defined as fever >38ºC with cough and chest radiography showing parenchymal lesion) with pleural effusion.
Exclusion criteria	Exclusion criteria Known drug allergy, immune-deficiency state, contraindications to steroid therapy, and other (unspecified) conditions precluding participation in the study.
Intervention(s)	The intervention group received 8 intravenous dexamethasone (0.25mg/kg 6 hourly) for 48 hours. All participants received the study medication (within 12 hours of diagnosis; and concomitant ranitidine and cefotaxime until 48 hours after the patient was afebrile, followed with co-amoxyclav). Children without complicated effusion were given medical management without a diagnostic pleural tap. The procedure was done only in those with effusion size >10 mm confirmed by ultrasonography. Pleural drainage and fibrinolytic therapy, or video-assisted thoracoscopic surgery (VATS) were reserved for children with complicated effusion. However the criteria for VATS referral are unclear

Comparator	The placebo group received a similar volume of normal saline in the same manner as the intervention arm. Placebo every 6 hours over 48 hours, plus antibiotics (ranitidine concomitantly and cefotaxime until 48 hours after the patient was afebrile, followed with co-amoxyclav).
Outcome measures	Adverse events Time to recovery All- cause mortality
Number of participants	60 children, ranging in age from 1 month to 14 years, with community acquired pneumonia (CAP) and pleural effusion.
Duration of follow-up	NR
Loss to follow-up	None. Of the 60 enrolled children, all were accounted for each of the outcomes
Methods of analysis	Sample size calculation was performed *a priori*, to detect a difference of 1 day for the primary outcome (time-to-recovery) assuming alpha error 5%, beta error 20%, and attrition of 10%. The calculated sample size was 28 in each group. Intention-to-treat (ITT) analysis was performed. Missing data were handled appropriately. Appropriate statistical methods were used.
Additional comments	In this study, 60% children in the treatment arm and 73% in the control arm had received at least 3 doses of pneumococcal conjugate vaccine. Despite this, the etiology was attributed to Pneumococcus in16% and 36%, respectively.

NR= not reported; CAP= community acquired pneumonia

Study arms

Intervention arm (N = 29)

intravenous dexamethasone (0.25 mg/kg/ dose) every 6 hours over 48 hours, plus antibiotics

Control arm (N = 29)

placebo every 6 hours over a period of 48 hours, along with antibiotics

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 (Double blinded trial using intention to treat analyses)

Section	Question	Answer
Overall bias and Directness	Overall Directness	Partially applicable *(Population indirectly applicable - Parapneumonic Pleural Effusion -)*

Wang, 2022

Bibliographic Reference	Wang, J.; Zhang, Y.; THE EFFECT OF METHYLPREDNISOLONE COMBINED WITH MACROLIDE ANTIBIOTICS ON MYCOPLASMA PNEUMONIAE PNEUMONIA IN CHILDREN; Farmacia; 2022; vol. 70 (no. 5); 850-854

Study details

Trial registration number and/or trial name	NR
Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	Department of Paediatrics, Zhejiang Provincial People's Hospital, Zhejiang
Study dates	July 2019 to October 2020
Sources of funding	NR
Inclusion criteria	The inclusion criteria were defined as follows: children diagnosed with MPP; children with complications such as atelectasis and pleural effusion; and children whose family members were informed of this study and volunteered to participate
Exclusion criteria	The exclusion criteria were defined as follows: children with low immune function; children combined with severe coagulation dysfunction and mental disorders; patients with tuberculosis infection, congenital heart disease, and other diseases; patients treated with other drugs within the past 1 month; and children with incomplete clinical data.
Intervention(s)	All children received macrolide antibiotics (MA) symptomatic, anti-infective, and supportive treatment. The intravenous infusion of erythromycin was injected once every 12 hours for 5 days. After erythromycin treatment, for 4 days the patients received no treatment and then they received azithromycin orally, 10 mg/kg bw/day for another 5 days. Children in the experimental group also received Methylprednisolone in the first 5 days, in doses of 2.0 mg/kg bw/day.
Comparator	The children in the control group received only macrolide antibiotics (MA) for symptomatic, anti-infective, and supportive treatment.
Outcome measures	Length of hospital stay Adverse events

Number of participants	60
Duration of follow-up	NR
Loss to follow-up	NR
Methods of analysis	Data analysis was done using SPSS 20.0 software. The count data were expressed as percentages, using Chi-squared (χ2) test; and the measurement data were expressed as media ± standard deviation ($\bar{x}\pm s$), using Student's t-test. A value of p < 0.05 meant that there was a statistically significant difference

NR= not reported; CAP= community acquired pneumonia

Study arms

Intervention group (N = 30)

MP + MA

Control group (N = 30)

MA only

Characteristics

Arm-level characteristics

Characteristic	Intervention group (N = 30)	Control group (N = 30)
Mean age (SD) Mean (SD)	6.5 (2.8)	6.8 (2.7)
No. of males No of events	n = 17 ; % = 56	n = 15 ; % = 43

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	Moderate Lack of information on methods process (randomisation, participant/assessor blinding)
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E – Forest plots

Adults

Corticosteroids vs usual care in adults with community-acquired pneumonia

Mortality: Number of patients who had died at longest follow-up or closest to 90 days.

See figure 2 from the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

180 day results from the STEP trial (Blum 2023) were consistent with the 30 day results, showing no significant difference between corticosteroids and usual care. Mortality for usual care = 25 (6.8%), corticosteroids = 35 (9.7%), RR 1.42 (0.87–2.32), P=0.601. This is unlikely to significantly alter the direction or magnitude of the pooled result.

Invasive mechanical ventilation: Number of patients who had needed to use a ventilator (who were not using a ventilator at baseline) at longest follow up or closest to 90 days.

See eFigure 8 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

ICU admission: Number of patients who had been admitted to ICU (who were not in ICU at baseline) at longest follow up or closest to 90 days.

See eFigure 14 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

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

See eFigure 15 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

Duration of ICU stay: Mean duration of ICU stay in days.

See eFigure 19 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

Ventilator free days: Mean duration without requiring use of a ventilator in days

See eFigure 23 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

Infections: Number of patients who had contracted a secondary infection by longest follow-up or closest to 90 days.

See eFigure 24 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

180 day results from the STEP trial (Blum 2023) differed from the 30 day results, showing a significant effect favouring usual care, rather than no significant difference between groups as shown in the forest plot. Secondary infections for usual care = 35 (9.6%), corticosteroids = 62 (17.2%) RR 1.78 (1.22–2.54), P=0.003. This is unlikely to significantly alter the direction or magnitude of the pooled result.

Gastrointestinal bleeds: Number of patients who had experienced gastrointestinal bleeding by longest follow-up or closest to 90 days.

See eFigure 28 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

Hyperglycaemia: Number of patients who had experienced Hyperglycaemia by longest follow-up or closest to 90 days.

See eFigure 32 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

Corticosteroids vs usual care in adults with community-acquired pneumonia: Subgroup analysis by duration of treatment <7 days versus ≥7 day

Mortality: Number of patients who had died by longest follow-up or closest to 90 days, subgroup analysis by duration of treatment <7 days versus ≥7 day

See eFigure 4 from supplementary file 1 of the Pitre (2023) review at doi.org/10.1007/s11606-023-08203-6

Invasive mechanical ventilation: Number of patients who had needed to use a ventilator (who were not using a ventilator at baseline) at longest follow up or closest to 90 days, subgroup analysis by duration of treatment <7 days versus ≥7 day

See eFigure 10 from supplementary file 1 of the Pitre (2023) review at

doi.org/10.1007/s11606-023-08203-6

ICU admission: Number of patients who had been admitted to ICU (who were not in ICU at baseline) at longest follow up or closest to 90 days, subgroup analysis by duration of treatment <7 days versus ≥7 day

See eFigure 13 from supplementary file 1 of the Pitre (2023) review at

doi.org/10.1007/s11606-023-08203-6

Duration of hospitalisation: Mean duration of hospital stay in days, subgroup analysis by duration of treatment <7 days versus ≥7 day

See eFigure 17 from supplementary file 1 of the Pitre (2023) review at

doi.org/10.1007/s11606-023-08203-6

Duration of ICU stay: Mean duration of ICU stay in days, subgroup analysis by duration of treatment <7 days versus ≥7 day

See eFigure 21 from supplementary file 1 of the Pitre (2023) review at

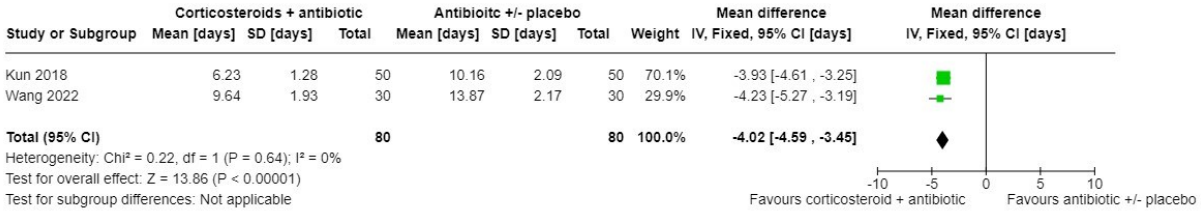
doi.org/10.1007/s11606-023-08203-6

Babies, children, and young people

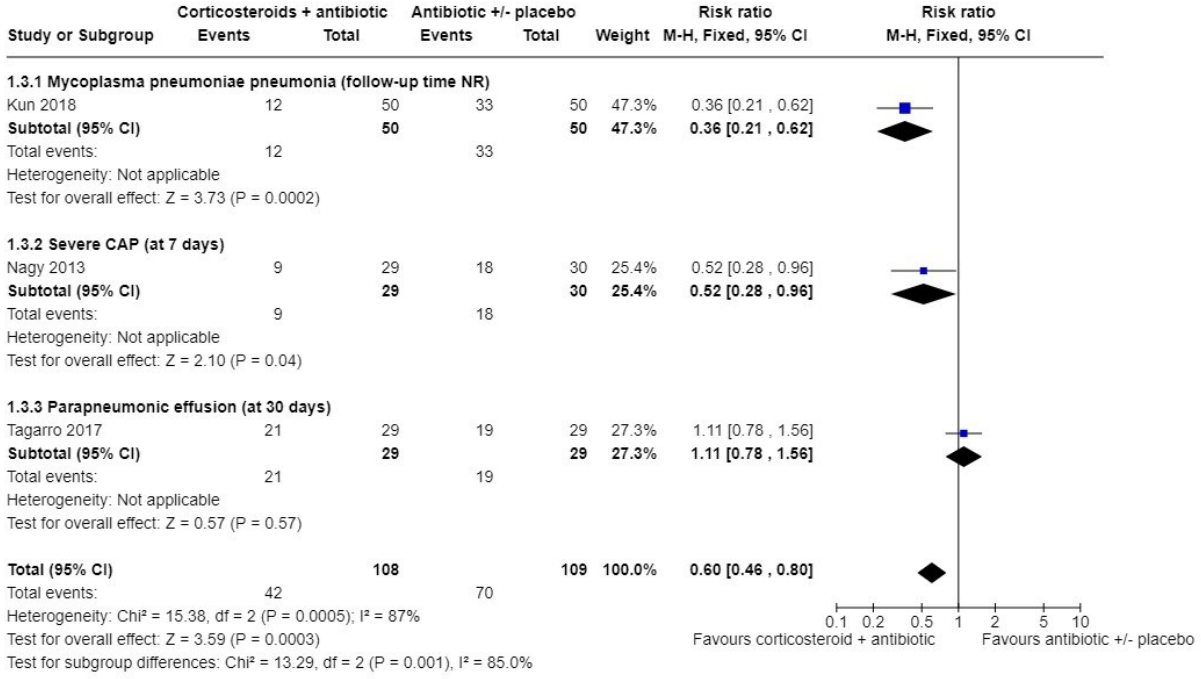
Corticosteroids + antibiotics vs antibiotics +/- placebo in babies children and young people

Analysis 1.1: Cure (all participants with mycoplasma pneumonia, follow up time not specified)

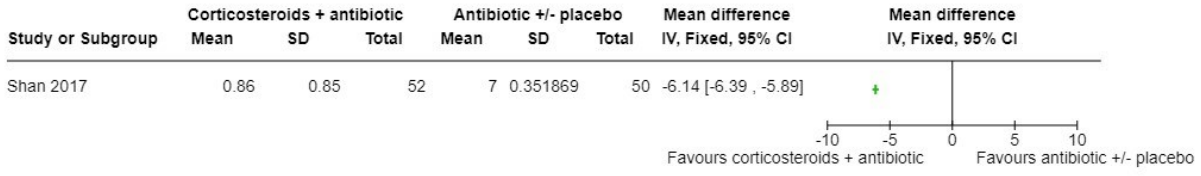
Analysis 1.2: Length of hospital stay (days, all participants with mycoplasma pneumonia)



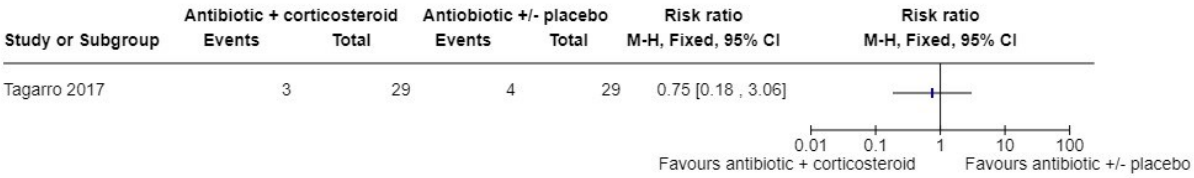
Analysis 1.3: Any adverse events



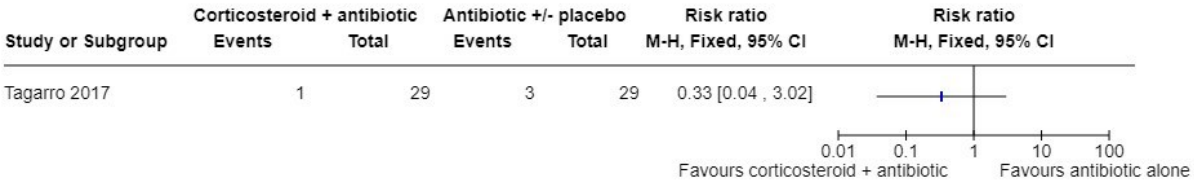
Analysis 1.4: Average febrile period (in days, all participants with refractory mycoplasma pneumonia)



Analysis 1.5: All-cause mortality (parapneumonic effusion, follow up time not specified)



Analysis 1.6: Progression of simple effusion requiring pleural drainage (parapneumonic effusion, days 1-3)



Appendix F – GRADE tables

RQ6.1a Community-acquired pneumonia in adults

No GRADE tables were produced for this review. The outcomes reported in Pitre (2023) and reproduced in the body of this review (table 4) give the summary GRADE assessment made by Pitre (2023).

RQ6.1b Hospital-acquired pneumonia in adults

No evidence identified.

RQ6.1c HAP and CAP in babies children and young people

Table 14: Corticosteroids + antibiotics compared to antibiotics +/- placebo for pneumonia in children and young people

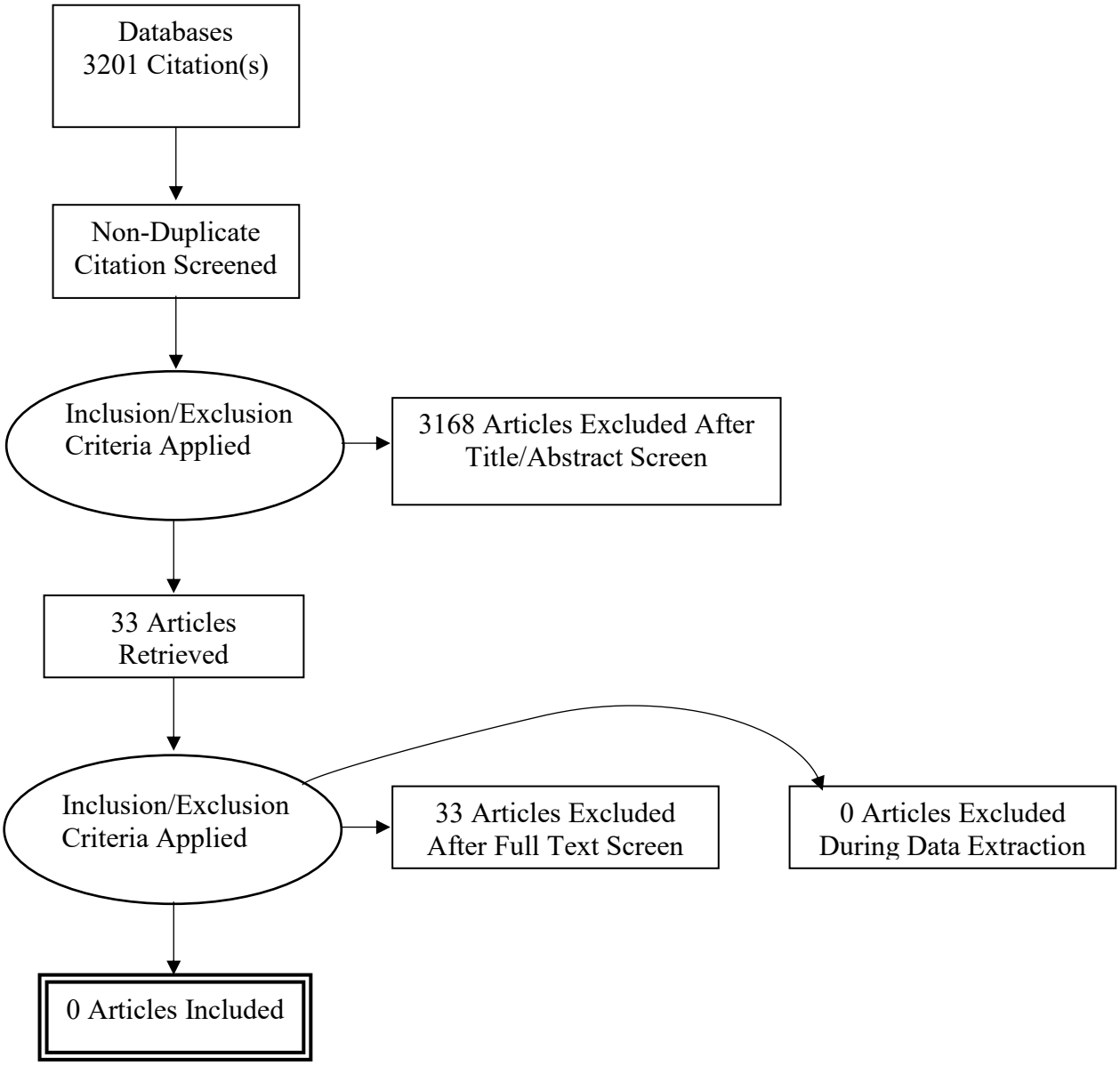
Certainty assessment						№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Corticosteroid + antibiotics**	**antibiotics +/- placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Cure (all participants with mycoplasma pneumonia, follow up time not specified, RR>1 favours corticosteroid + antibiotic)										
2[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	38/80 (47.5%)	28/80 (35.0%)	**RR 1.36** (0.93 to 1.98)	**126 more per 1,000** (from 24 fewer to 343 more)	⨁⨁◯◯ Low
Any adverse events – total (see subgroups in forest plots for follow up times , RR<1 favours corticosteroid + antibiotic)										
3[d]	randomised trials	serious[b]	very serious[e]	not serious	serious[f]	42/108 (38.9%)	70/109 (64.2%)	**RR 0.60** (0.46 to 0.80)	**257 fewer per 1,000** (from 347 fewer to 128 fewer)	⨁◯◯◯ Very low
Average febrile period (days, all participants with refractory mycoplasma pneumonia, days fewer favours corticosteroid + antibiotic)										

Certainty assessment						№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Corticosteroid + antibiotics**	**antibiotics +/- placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
1[g]	randomised trials	very serious[h]	serious[i]	not serious	not serious	52	50	-	MD **6.14 days fewer** (6.39 fewer to 5.89 fewer)	⨁◯◯◯ Very low
All-cause mortality (parapneumonic effusion, follow up time not specified, RR<1 favours corticosteroid + antibiotic)										
1[j]	randomised trials	not serious	serious[i]	not serious	very serious[k]	3/29 (10.3%)	4/29 (13.8%)	**RR 0.75** (0.18 to 3.06)	**34 fewer per 1,000** (from 113 fewer to 284 more)	⨁◯◯◯ Very low
Progression of simple effusion requiring pleural drainage (parapneumonic effusion, days 1-3, , RR<1 favours corticosteroid + antibiotic)										
1[j]	randomised trials	not serious	serious[i]	not serious	very serious[k]	1/29 (3.4%)	3/29 (10.3%)	**RR 0.33** (0.04 to 3.02)	**69 fewer per 1,000** (from 99 fewer to 209 more)	⨁◯◯◯ Very low
Time to recovery (all participants with parapneumonic effusion, HR>1 favours corticosteroid + antibiotic)										

Certainty assessment						№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Corticosteroid + antibiotics**	**antibiotics +/- placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
1[j]	randomised trials	serious[l]	serious[i]	not serious	very serious[k]	30 participants	30 participants	-	**Median difference 68 hours shorter (38%)**	⨁◯◯◯ Very low
Length of hospital stay (days, all participants with mycoplasma pneumonia, days fewer favours corticosteroid + antibiotic))										
2[a]	randomised trials	serious[b]	not serious	not serious	not serious	80	80	-	MD **0.402 days fewer** (4.59 fewer to 3.45 fewer)	⨁⨁⨁◯ Moderate

a. Kun 2018, Wang 2022
b. Downgraded once as greater than 33.3% of the weight in the meta-analysis came from studies at moderate or high risk of bias
c. Downgraded once as 95%CI crosses one clinical decision threshold (1.25)
d. Kun 2018, Nagy 2013, Tagarro 2017
e. Downgraded twice as the I2 was greater than 66.7% (I2 = 87%)
f. Downgraded once as 95%CI crosses one clinical decision threshold (0.8)
g. Shan 20117
h. Downgraded twice for serious risk of bias: major limitation of the trial was its "open" design, thus cross-contamination cannot be ruled out. Because there is no placebo control group, a placebo effect cannot be excluded.
i. Downgraded once for inconsistency: single study
j. Tagarro 2017
k. Downgraded twice because 95%CI crosses 2 clinical decision thresholds (0.8 and 1.25)
l. Downgraded once for moderate risk of bias

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

Excluded studies for RQ6.1a Community-acquired pneumonia in adults

Study	Reason for exclusion
Bangonda, P.R., Dinesh, N., Kurian, T.P. et al. (2024) Corticosteroids on Severe Community-Acquired Pneumonia. International Journal of Pharmaceutical and Clinical Research 16(9): 401-403	- Systematic review containing no new studies
Chaudhuri, D., Nei, A.M., Rochwerg, B. et al. (2024) 2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia. Critical Care Medicine 52(5): e219-e233	- Not a relevant study design *Non-experimental*
Chaudhuri, Dipayan, Israelian, Lori, Putowski, Zbigniew et al. (2024) Adverse Effects Related to Corticosteroid Use in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia: A Systematic Review and Meta-Analysis. Critical care explorations 6(4): e1071	- Systematic review containing no new studies
Chen, LP, Chen, JH, Chen, Y et al. (2015) Efficacy and safety of glucocorticoids in the treatment of community-acquired pneumonia: a meta-analysis of randomized controlled trials. World journal of emergency medicine 6(3): 172-178	- Duplicate reference
Dequin, Pierre-Francois, Meziani, Ferhat, Quenot, Jean-Pierre et al. (2023) Hydrocortisone in Severe Community-Acquired Pneumonia. The New England journal of medicine 388(21): 1931-1941	- Duplicate reference
Diaz Caballero, Luis A, Aijaz, Ashnah, Saleem Paryani, Neha et al. (2024) Comparing the efficacy of corticosteroids among patients with community-acquired pneumonia in the ICU versus non-ICU settings: A systematic review and meta-analysis. Steroids 205: 109389	- Systematic review containing no new studies
Guo, K.; Yadav, K.; Rosenberg, H. (2023) Hydrocortisone in severe community-acquired pneumonia. Canadian Journal of Emergency Medicine 25(8): 656-658	- Review article but not a systematic review *Commentary on article*
Heming, Nicholas, Renault, Alain, Kuperminc, Emmanuelle et al. (2024) Hydrocortisone plus fludrocortisone for community acquired pneumonia-related septic shock: a subgroup analysis of the APROCCHSS phase 3 randomised trial. The Lancet. Respiratory medicine 12(5): 366-374	- Excluded population *Sepsis*
Lanthier, L, Mayette, M, Plourde, M-E et al. (2023) In adults admitted to the intensive care unit for severe community-acquired pneumonia, does adding hydrocortisone to standard treatment reduce 28-days mortality compared to placebo, and is it safe?. Revue de medecine interne 44(7): 383-384	- Study not reported in English

Study	Reason for exclusion
Pitre, Tyler, Abdali, Daniyal, Chaudhuri, Dipayan et al. (2023) Corticosteroids in Community-Acquired Bacterial Pneumonia: a Systematic Review, Pairwise and Dose-Response Meta-Analysis. Journal of general internal medicine 38(11): 2593-2606	- Duplicate reference
See, Xin Ya, Wang, Tsu Hsien, Chang, Yu-Cheng et al. (2024) Impact of different corticosteroids on severe community-acquired pneumonia: a systematic review and meta-analysis. BMJ open respiratory research 11(1)	- Systematic review containing no new studies
Tachiwada, T Noguchi, S Muramatsu, K Akata, K Yamasaki, K Kido, T Asakawa, T Fujino, Y Fushimi, K Matsuda, S Mukae, H Yatera, K (2022) Effects of additive corticosteroid therapy on 90-day survival in patients with community-onset pneumonia. JOURNAL OF INFECTION AND CHEMOTHERAPY 28(4): 496 - 503	- Not a relevant study design *Retrospective, not RCT*
Wang, Donglan and Zhu, Yan (2024) The Complications of Corticosteroid for Patients with Community-acquired Pneumonia: A Systematic Review and Meta-Analysis. Alternative therapies in health and medicine 30(11)	- Systematic review containing no new studies
Wittermans, E van de Garde, EMW Voorn, GP Aldenkamp, AF Janssen, R Grutters, JC Bos, WJW (2022) Neutrophil count, lymphocyte count and neutrophil-to-lymphocyte ratio in relation to response to adjunctive dexamethasone treatment in community-acquired pneumonia. EUROPEAN JOURNAL OF INTERNAL MEDICINE 96: 102 - 108	- Secondary publication of an included study that does not provide any additional relevant information *Additional post-hoc analysis*
Wittermans, E van der Zee, PA Qi, HC van de Garde, EMW Blum, CA Christ-Crain, M Gommers, D Grutters, JC Voorn, GP Bos, WJW Endeman, H (2022) Community-acquired pneumonia subgroups and differential response to corticosteroids: a secondary analysis of controlled studies. ERJ OPEN RESEARCH 8(1)	- Secondary publication of an included study that does not provide any additional relevant information
Zhao, J.; Pan, X.; Shao, P. (2024) Meta-analysis of combined azithromycin and inhaled budesonide treatment for Chinese pediatric patients with mycoplasma pneumonia. Medicine (United States) 103(24): e38332	- Excluded population *Under 18*

Excluded studies for RQ6.1b Hospital-acquired pneumonia in adults

Study	Reason for exclusion
Nedel, Wagner Luis, Nora, David Garcia, Salluh, Jorge Ibrain Figueira et al. (2016) Corticosteroids for severe influenza pneumonia: A critical appraisal. World journal of critical care medicine 5(1): 89-95	- Systematic review used as source of primary studies *No RCTs*

Study	Reason for exclusion
Stern, Anat, Skalsky, Keren, Avni, Tomer et al. (2017) Corticosteroids for pneumonia. The Cochrane database of systematic reviews 12: cd007720	- Systematic review used as source of primary studies *No relevant studies*
Tang, Qiufeng, Chen, Qiongyan, Li, Yanqing et al. (2022) Association between Glucocorticoids and Mortality in Patients with Severe Pneumonia: A Systematic Review and Meta-Analysis Based on Randomized Controlled Trials. Computational and mathematical methods in medicine 2022: 1191205	- Systematic review used as source of primary studies *Studies only included HAP as a secondary infection.*
Zhou, Yuqing, Fu, Xiaofang, Liu, Xiaoxiao et al. (2020) Use of corticosteroids in influenza-associated acute respiratory distress syndrome and severe pneumonia: a systemic review and meta-analysis. Scientific reports 10(1): 3044	- Systematic review used as source of primary studies *No HAP studies*

Excluded studies for RQ6.1c HAP and CAP in babies, children, and young people

Study	Reason
Blum, Claudine Angela Nigro, Nicole Briel, Matthias Schuetz, Philipp Ullmer, Elke Suter-Widmer, Isabelle Winzeler, Bettina Bingisser, Roland Elsaesser, Hanno Drozdov, Daniel Arici, Birsen Urwyler, Sandrine Andrea Refardt, Julie Tarr, Philip Wirz, Sebastian Thomann, Robert Baumgartner, Christine Duplain, Herve Burki, Dieter Zimmerli, Werner Rodondi, Nicolas Mueller, Beat Christ-Crain, Mirjam (2015) Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. LANCET 385(9977): 1511 - 1518	- Duplicate reference
Buendia, Jefferson A. 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	- Study does not contain a relevant intervention *Cost effectiveness data*
Cheema, Huzaifa Ahmad, Musheer, Adeena, Ejaz, Arooba et al. (2023) Efficacy and safety of corticosteroids for the treatment of community-acquired pneumonia: A systematic review and meta-analysis of randomized controlled trials. Journal of critical care 80: 154507	- Does not contain a population of people of CYP *Adults only*
Chen, YL Dong, SW Tian, L Chen, HS Chen, J He, CZ (2022) Combination of azithromycin and methylprednisolone alleviates Mycoplasma pneumoniae induced pneumonia by regulating miR-	- Not a relevant study design *Clinical sample analysis*

Study	Reason
499a-5p/STAT3 axis. EXPERIMENTAL AND THERAPEUTIC MEDICINE 24(3)	
Chetty, Krishne Thomson, Anne H (2007) Management of community-acquired pneumonia in children. Paediatric drugs 9(6): 401 - 11	- Not a relevant study design
Confalonieri, M Urbino, R Potena, A Piattella, M Parigi, P Puccio, G Della Porta, R Giorgio, C Blasi, F Umberger, R Meduri, GU (2005) Hydrocortisone infusion for severe community-acquired pneumonia - A preliminary randomized study. AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 171(3): 242 - 248	- Does not contain a population of people of CYP *Adults only*
Delara, Mahin, Chauhan, Bhupendrasinh F, Le, Me-Linh et al. (2019) Efficacy and safety of pulmonary application of corticosteroids in preterm infants with respiratory distress syndrome: a systematic review and meta-analysis. Archives of disease in childhood. Fetal and neonatal edition 104(2): f137-f144	- Does not contain a population of people within the age limits *New born babies*
Du, X F, Meng, L M, Niu, W Z et al. (2016) Clinic observation of 41 cases of Pingchuan Zhike Tie adjuvant therapy for pediatric mycoplasma pneumonia cough. Journal of pediatrics of traditional chinese medicine [zhong yi ER ke za zhi] 12(2): 32-34	- Study does not contain a relevant intervention
Duan, Y.; Zhou, H.; Chen, J. (2021) The effects of the atomization inhalation of budesonide, salbutamol, and ipratropium bromide on the t-lymphocyte subset and inflammatory cytokine levels in children with asthmatic pneumonia. American Journal of Translational Research 13(9): 10517-10526	- Study does not contain a relevant intervention *Not an adjunct to antibiotics*
Fernandes, Ricardo M, Oleszczuk, Marta, Woods, Charles R et al. (2014) The Cochrane Library and safety of systemic corticosteroids for acute respiratory conditions in children: an overview of reviews. Evidence-based child health : a Cochrane review journal 9(3): 733-47	- Does not contain a population of people with pneumonia *No reviews included on pneumonia*
Fernandes, Ricardo M, Wingert, Aireen, Vandermeer, Ben et al. (2019) Safety of corticosteroids in young children with acute respiratory conditions: a systematic review and meta-analysis. BMJ open 9(8): e028511	- Does not contain a population of people with pneumonia receiving antibiotic treatment. *Not pneumonia specific, but also because it does not require people to be on an antibiotic, which is one of our protocol criteria*
Fitzgerald, DB Waterer, GW Budgeon, C Shrestha, R Fysh, ET Muruganandan, S Stanley, C Saghaie, T Badiei, A Sidhu, C Harryanto, H Duong, V Azzopardi, M Manners, D Lan, NSH Popowicz, ND Peddle-McIntyre, CJ Rahman,	- Does not contain a relevant population *Adults*

Study	Reason
NM Read, CA Tan, AL Gan, SK Murray, K Lee, YCG (2022) Steroid Therapy and Outcome of Parapneumonic Pleural Effusions (STOPPE) A Pilot Randomized Clinical Trial. AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 205(9): 1093 - 1101	
Gong, L., Xu, L., Diao, M. et al. (2016) Clinical effect of treating secondary asthma attacks of children Mycoplasma pneumoniae with combined therapy of montelukast and azithromycin. European Review for Medical and Pharmacological Sciences 20(24): 5256-5260	- Does not contain a population of people with pneumonia
Horita, N Otsuka, T Haranaga, S Namkoong, H Miki, M Miyashita, N Higa, F Takahashi, H Yoshida, M Kohno, S Kaneko, T (2015) Adjunctive Systemic Corticosteroids for Hospitalized Community-Acquired Pneumonia: Systematic Review and Meta-Analysis 2015 Update. SCIENTIFIC REPORTS 5	- Does not contain a population of CYP *Adults only*
Huang, Lizhen; Gao, Xiang; Chen, Meiyuan (2014) Early treatment with corticosteroids in patients with Mycoplasma pneumoniae pneumonia: a randomized clinical trial. Journal of tropical pediatrics 60(5): 338-42	- Comparator in study does not match that specified in protocol
Hume-Nixon, Maeve, Graham, Hamish, Russell, Fiona et al. (2022) Review of the role of additional treatments including oseltamivir, oral steroids, macrolides, and vitamin supplementation for children with severe pneumonia in low- and middle-income countries. Journal of global health 12: 10005	- Systematic review used as source of primary studies
Kim, Hwan Soo, Sol, In Suk, Li, Donghe et al. (2019) Efficacy of glucocorticoids for the treatment of macrolide refractory mycoplasma pneumonia in children: meta-analysis of randomized controlled trials. BMC pulmonary medicine 19(1): 251	- Systematic review used as source of primary studies
Kohns Vasconcelos, Malte, Meyer Sauteur, Patrick M, Keitel, Kristina et al. (2023) Detection of mostly viral pathogens and high proportion of antibiotic treatment initiation in hospitalised children with community-acquired pneumonia in Switzerland - baseline findings from the first two years of the KIDS-STEP trial. Swiss medical weekly 153: 40040	- *No outcomes of interest reported*
Kohns Vasconcelos, Malte, Meyer Sauteur, Patrick M, Santoro, Regina et al. (2020) Randomised placebo-controlled multicentre effectiveness trial of adjunct betamethasone therapy in hospitalised children with community-acquired pneumonia: a trial protocol for the KIDS-STEP trial. BMJ open 10(12): e041937	- Not a relevant study design *Trial protocol*
Lee, Jan Hau Loh, Tsee Foong (2010) Continuous hydrocortisone infusion in severe pediatric community-	- Not a relevant study design *Case report*

Study	Reason
acquired pneumonia (CAP). PEDIATRICS INTERNATIONAL 52(3): e125 - e127	
Li, Y., Yang, W., Wu, X. et al. (2022) Effect of bronchofiberscopic lavage with budesonide suspension on refractory mycoplasma pneumoniae pneumonia. Pakistan Journal of Medical Sciences 38(4): 922-927	- Comparator in study does not match that specified in protocol
Liu, Bo, Li, Song-Qin, Zhang, Su-Ming et al. (2013) Risk factors of ventilator-associated pneumonia in pediatric intensive care unit: a systematic review and meta-analysis. Journal of thoracic disease 5(4): 525-31	- Study does not contain a relevant intervention
Luo, Zhengxiu, Luo, Jian, Liu, Enmei et al. (2014) Effects of prednisolone on refractory mycoplasma pneumoniae pneumonia in children. Pediatric pulmonology 49(4): 377-80	- *No outcomes of interest reported*
Lv, Jun and Fan, Fei (2022) Efficacy of Methylprednisolone plus Azithromycin in the Treatment of RMPP and Its Effect on the Changes of T Lymphocyte Subsets. Evidence-based complementary and alternative medicine : eCAM 2022: 1833195	*No outcomes of interest reported*
Marks, M I, Chicoine, L, Legere, G et al. (1972) Adrenocorticosteroid treatment of hydrocarbon pneumonia in children--a cooperative study. The Journal of pediatrics 81(2): 366-9	- Does not contain a revelant population *Subjects had a history of hydrocarbon poisoning*
McHardy, V U and Schonell, M E (1972) Ampicillin dosage and use of prednisolone in treatment of pneumonia: co-operative controlled trial. British medical journal 4(5840): 569-73	- Does not contain a population of CYP *Adults*
Mukanhaire, L., Wang, J., Zong, X. et al. (2022) Recent advances in efficacy of corticosteroids as adjunct therapy for the treatment of community-acquired pneumonia in children: a systematic review and meta-analysis. medRxiv	- Not a relevant study design *protocol*
Newberry, L., O'Hare, B., Kennedy, N. et al. (2017) Early use of corticosteroids in infants with a clinical diagnosis of Pneumocystis jiroveci pneumonia in Malawi: a double-blind, randomised clinical trial. Paediatrics and International Child Health 37(2): 121-128	- Does not contain a relevant population *HIV infected subjects*
Parikh, Nehal A, Locke, Robert G, Chidekel, Aaron et al. (2004) Effect of inhaled corticosteroids on markers of pulmonary inflammation and lung maturation in preterm infants with evolving chronic lung disease. The Journal of the American Osteopathic Association 104(3): 114-20	- Does not contain a population of people within the age limit *Infants <28 days old*
Pljaskic Kamenov, S; Filipovic, M; Kamenov, B (2000) The role of methylprednisolone in the treatment of pneumonia in school children. Respir-med 94suppla: A.11-2	- Conference abstract

Study	Reason
Principi, N Bianchini, S Baggi, E Esposito, S (2013) No evidence for the effectiveness of systemic corticosteroids in acute pharyngitis, community-acquired pneumonia and acute otitis media. EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY & INFECTIOUS DISEASES 32(2): 151 - 160	- Review article but not a systematic review *Checked included studies only 3 relevant to children, non RCTS*
Qiu, Jian-Li, Huang, Li, Shao, Ming-Yi et al. (2020) Efficacy and safety of azithromycin combined with glucocorticoid on refractory Mycoplasma pneumoniae pneumonia in children: A PRISMA-compliant systematic review and meta-analysis. Medicine 99(22): e20121	- Systematic review used as source of primary studies
Saleem, N Kulkarni, A Snow, TAC Ambler, G Singer, M Arulkumaran, N (2023) Effect of Corticosteroids on Mortality and Clinical Cure in Community-Acquired Pneumonia A Systematic Review, Meta-analysis, and Meta-regression of Randomized Control Trials. CHEST 163(3): 484 - 497	- Does not contain a relevant population *Adults*
Shen, Huanan; Zhao, Xingni; Xu, Liangyin (2023) Meta-analysis of the efficacy of budesonide and ambroxol hydrochloride inhalation in children with pneumonia and their effects on inflammatory response. Heliyon 9(11): e21105	- Systematic review used as source of primary studies
Sibila, O. Agusti, C. Torres, A. (2008) Corticosteroids in severe pneumonia. EUROPEAN RESPIRATORY JOURNAL 32(2): 259 - 264	- Review article but not a systematic review
Snijders, Dominic Daniels, Johannes M. A. de Graaff, Casper S. van der Werf, Tjip S. Boersma, Wim G. (2010) Efficacy of Corticosteroids in Community-acquired Pneumonia A Randomized Double-Blinded Clinical Trial. AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 181(9): 975 - 982	- Does not contain a population of CYP *Adults only*
Stern, Anat, Skalsky, Keren, Avni, Tomer et al. (2017) Corticosteroids for pneumonia. The Cochrane database of systematic reviews 12: cd007720	- Systematic review used as source of primary studies
Sun, Lin-Li, Ye, Chao, Zhou, Yu-Lu et al. (2020) Meta-analysis of the Clinical Efficacy and Safety of High- and Low-dose Methylprednisolone in the Treatment of Children With Severe Mycoplasma Pneumoniae Pneumonia. The Pediatric infectious disease journal 39(3): 177-183	- Comparator in study does not match that specified in protocol *not an eligible comparator; comparator should be no steroids*
Terblanche, Alta J, Green, Robin J, Rheeder, Paul et al. (2008) Adjunctive corticosteroid treatment of clinical Pneumocystis jiroveci pneumonia in infants less than 18 months of age--a randomised controlled trial. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde 98(4): 287-90	- Does not contain a relevant population *HIV subjects*

Study	Reason
Wu, YJ, Sun, J, Zhang, JH et al. (2014) Clinical efficacy of adjuvant therapy with glucocorticoids in children with lobar pneumonia caused by Mycoplasma pneumoniae. Zhongguo dang dai er ke za zhi [Chinese journal of contemporary pediatrics] 16(4): 401-405	- Full text paper not available
Xu, Baoping, Peng, Xiaoxia, Yao, Yao et al. (2018) Low-dose versus high-dose methylprednisolone for children with severe Mycoplasma pneumoniae pneumonia (MCMP): Study protocol for a randomized controlled trial. Pediatric investigation 2(3): 176-183	- Not a relevant study design *protocol*
Yang, XY Jin, H (2022) Safety of corticosteroids in the treatment of acute respiratory disease in children: a systematic review and meta-analysis. TRANSLATIONAL PEDIATRICS 11(2): 194 - 203	- Systematic review with no new studies
Ye, J., Ye, H., Wang, M. et al. (2021) Total serum IL-6 and TNF-C levels in children with bronchopneumonia following treatment with methylprednisolone in combination with azithromycin. American Journal of Translational Research 13(8): 9458-9464	- Comparator in study does not match that specified in protocol *Does not fit - abx + steroid vs abx alone.*
Zhao, J.; Pan, X.; Shao, P. (2024) Meta-analysis of combined azithromycin and inhaled budesonide treatment for Chinese pediatric patients with mycoplasma pneumonia. Medicine (United States) 103(24): e38332	- Study not reported in English *SR of studies unavailable in English, evidence cannot be verified.*
Zhao, QC Yang, JB Sheng, YM Zhuang, M Qi, M (2022) Study on the Therapeutic Effect of Azithromycin Combined with Glucocorticoid on Pulmonary Function and Inflammatory Response in Children with Pneumonia. JOURNAL OF HEALTHCARE ENGINEERING 2022	- population *New evidence on Mycoplasma pneumonia not required by committee*

CAP= community acquired pneumonia; HAP= hospital acquired pneumonia; CYP= children and young people

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*
Cisco, Giulio, Meier, Armando N, Senn, Nicolas et al. (2024) Cost-effectiveness analysis of procalcitonin and lung ultrasonography guided antibiotic prescriptions in	- setting in primary care whereas the review was in secondary care

Study	Code [Reason]
primary care. The European journal of health economics : HEPAC : health economics in prevention and 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*
McKinnell, James A, Corman, Shelby, Patel, Dipen et al. (2018) Effective Antimicrobial Stewardship Strategies for Cost-effective Utilization of Telavancin for the Treatment	- Study does not contain a relevant intervention

Study	Code [Reason]
of Patients With Hospital-acquired Bacterial Pneumonia Caused by Staphylococcus aureus. Clinical therapeutics 40(3): 406-414e2	*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 Community Acquired Pneumonia: A Retrospective,	- Study does not contain a relevant intervention *Andrographolide Sulfonate injection*

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

Appendix L– Research recommendations – full details

L1.1 Research recommendation

In people hospitalised with community-acquired pneumonia (CAP) or hospital acquired pneumonia (HAP), what is the most effective and cost-effective corticosteroid treatment (as an adjunct to antibiotics), including dose, duration, and route of administration, and does the pathogen involved have an impact on efficacy?

L1.1.1 Why this is important

It has been demonstrated that a course of corticosteroids in addition to antibiotics is effective in reducing mortality and improving outcomes in adults hospitalised with severe CAP, but the evidence did not establish which corticosteroid, dose, duration or route of administration was most effective, nor whether the pathogen had an impact on efficacy. There was also no evidence for HAP, and limited evidence for babies, children and young people, so these groups are included in the PICO because further evidence is required for them.

L1.1.2 Rationale for research recommendation

Importance to 'patients' or the population	Patients receiving treatment with corticosteroids need to be given the optimum type, dose and duration of treatment. In addition, there is insufficient information on the benefits of corticosteroids in HAP, or in children, and because of the side-effects of corticosteroids it is important to be able to balance the risks and benefits before making a decision about whether to recommend them.
Relevance to NICE guidance	There was insufficient evidence to inform a decision for this guideline about whether or not to recommend corticosteroids as an adjunct to antibiotics for people with HAP or for babies, children, and young people with HAP or CAP. The recommendation on corticosteroid type and duration was made by committee consensus; evidence is required to further strengthen this.
Relevance to the NHS	A better understanding of the balance of risks and benefits of prescribing corticosteroids specific to each population and targeted at specific pathogens (e.g. pneumococcal pneumonia vs legionella vs MRSA vs klebsiella) might enable a more targeted and cost-effective intervention which may speed recovery and reduce mortality. Clinicians need guidance on drug and dosing information when implementing recommendations.
National priorities	Moderate
Current evidence base	Poor
Equality considerations	Pneumonia may be associated with socioeconomic deprivation and is also more common in people with some chronic illnesses.

L1.1.3 Modified PICO table

Population	Babies (over 28 days corrected gestational age, children and young people (<18 years), hospitalised with CAP or HAP. Adults hospitalised with CAP or HAP.
Intervention	Antibiotic treatment plus a corticosteroid regime
Comparator	Antibiotic treatment plus an alternative corticosteroid regime
Outcome	• Mortality • Clinical cure • Length of hospital stay • Adverse events (including steroid related events such as secondary infections, GI bleeding or hyperglycaemia requiring treatment) • Cost-effectiveness
Study design	RCT
Timeframe	Short term
Additional information	Sub-group by: • Age • Pathogen • CAP/HAP • Corticosteroid type, dose, duration and route of administration