National Institute for Health and Care Excellence

Pneumonia: diagnosis and management (update)

[D] Evidence review for short courses of antibiotics compared to longer courses of antibiotics for babies, children and young people with community-acquired pneumonia

NICE guideline [number]

Evidence reviews underpinning recommendations 1.5.4 to 1.5.6 and research recommendations in the NICE guideline

April 2025

Draft for consultation

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

ISBN: xxx

Contents

1 The clinical and cost-effectiveness of shorter durations of antibiotic treatment compared to longer antibiotic treatment courses for babies, children and young people with community-acquired pneumonia.

1.1 Review question

Are shorter durations of antibiotic treatment effective and cost-effective at treating babies, children and young people with community-acquired pneumonia compared to longer treatment courses?

1.1.1 Introduction

The determining of the optimal duration of antibiotic treatment ensures the balance between providing an effective outcome for the individual and not requiring them to be taking treatment for any longer than it is necessary. The scoping process for this pneumonia guideline update indicated that for babies, children and young people there was some evidence to suggest that shorter (<5 days) treatment may be similarly effective to longer treatment. This review considers this evidence. Furthermore, providing guidance on the optimal duration of antibiotic treatment may contribute to the aims of antimicrobial stewardship.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	Babies over 28 days (corrected gestational age), children and young people (age <18 years) with CAP. CAP is defined as pneumonia that is acquired outside hospital. Exclusion: • Babies up to and including 28 days (corrected gestational age). • People with COVID-19 pneumonia. • People who acquire pneumonia while intubated (ventilator-associated pneumonia). • People who are severely immune-compromised (have a primary immune deficiency or secondary immune deficiency related to HIV infection, or severe drug or systemic disease-induced immunosuppression, for example, people who have

	taken immunosuppressant cancer therapy or undergone organ transplantation). • People in whom pneumonia is an expected terminal event. • People with non-pneumonic infective exacerbations of bronchiectasis. • People with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • People with pneumonia associated with cystic fibrosis. • People with aspiration pneumonia as a result of inhaling a large bolus of gastric contents.
Interventions	**Shorter duration of treatment (<5 days)** Antibiotic treatment for CAP – any of the below alone or in combination: • macrolides (including ketolides) • beta-lactams (cephalosporins and penicillins), subdivided into: ○ narrow-spectrum beta-lactams: ▪ class 1: penicillin G (benzylpenicillin), phenoxymethylpenicillin (penicillin V) ▪ class 2: ampicillin, amoxicillin ○ broad-spectrum beta-lactams: ▪ beta-lactamase stable penicillins: co-amoxiclav, piperacillin-tazobactam, timentin (ticarcillin-clavulanic acid), flucloxacillin, co-fluampicil ▪ cephalosporins • tetracyclines • respiratory fluoroquinolones.
Comparator	**Longer duration of treatment (≥5 days)** Any agent from the above classes compared for different durations
Outcomes	• Clinical cure at the end of follow up • Mortality at any time point • Need for invasive ventilation • ICU admission and duration of ICU stay • Hospital admission and duration of hospital stay • Treatment-related adverse events • Health-related quality of life
Study type	RCTs

CAP=community acquired pneumonia; HIV=human immunodeficiency virus; ICU=intensive care unit; RCT=randomised controlled trial

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, including

the use of the included systematic review, 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 5 systematic reviews which matched the inclusion criteria for this review. Of these 5, one systematic review was both recent and a close match:

> Gao, Y., Liu, M., Yang, K., Zhao, Y., Tian, J., Pernica, J. M., & Guyatt, G. (2023). Shorter Versus Longer-term Antibiotic Treatments for Community-Acquired Pneumonia in Children: A Meta-analysis. *Pediatrics*, *151*(6), e2022060097. https://doi.org/10.1542/peds.2022-060097

The committee agreed that this review directly addresses the review question, was up to date and was thorough. For this reason, to repeat it would be a duplication of effort. They noted that the searches were last run in April 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 review in its entirety was initially presented to the committee, using the analyses and GRADE that were conducted by Gao (2023), which 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.

Upon further discussion the committee requested that the review be altered to remove the 5 days vs 10 days comparisons to aid clarity in deciding how many days of antibiotics to recommend and to align the review with the protocol. This alteration was carried out by the NICE team, by removing the data from 4 studies from the analysis. The data and analyses for all other comparisons were retained as presented in Gao (2023), but pooled estimates for shorter vs longer durations combining these comparisons were recalculated. The GRADE assessment applied by Gao (2023) was also retained except where changes were necessary to apply to the recalculated effects.

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 run on 4 April 2024 and re-run on 17 October 2024 in order to update the searches done for Gao et al. (2023) that had been completed on 30 April 2022. The update search used the same databases as Gao et al.: Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley); Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCOhost); Embase (Ovid); and MEDLINE ALL (Ovid). The same study-type filters were applied as Gao et al. to identify randomised controlled trials. The same limits were applied, with an additional date limit for April 2022 to current. The

database searches were supplemented with forward citation searching conducted on Web of Science Core Collection on 4 April 2024 and 17 October 2024 using Gao et al. as a seed reference.

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). Limits were applied to remove animal studies, case reports, conference abstracts, editorials, letters, news items and references not published in the English language. The validated NICE Cost Utility Filter was used on MEDLINE and Embase. Validated NICE filters were used in MEDLINE and Embase to remove references exclusively set in countries that are not OECD members.

A NICE senior information specialist (SIS) conducted the searches. The Gao et al. searches were quality assured by a NICE SIS and minor amendments were made to the update searches. The MEDLINE strategies were quality assured and all translated search strategies were peer reviewed to ensure their accuracy. These 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 Gao (2023) in April 2022 were repeated to identify potentially relevant studies that had been published since the original search. This search found 333 references (see appendix B for the literature search strategy).

These 333 references were screened at title and abstract level against the review protocol, with 313 excluded at this level. 10% of references were screened separately by two reviewers with 100% agreement.

The full texts of 20 RCTs were ordered for closer inspection. None of these studies met the criteria specified in the review protocol (appendix A). The clinical evidence study selection is presented as a PRISMA diagram in appendix C.

Of the 16 studies analysed by Gao (2023), 4 were not selected for this review because they looked at antibiotic durations that did not fit the protocol and 1 was not selected because the original study source was an abstract rather than a full publication. For a summary of the 11 included studies from Gao (2023) see Table 3.

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

1.1.4.2 Excluded studies

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

1.1.5 Summary of studies included in the effectiveness evidence

Table 2: Summary of systematic review included in the effectiveness evidence

Study details	Population	Intervention	Comparison	Outcomes	Risk of bias (RoB)
Gao (2023) Systematic review and meta-analysis 16 studies in total. 11 Studies included in this review	Total N = 7,824 in the 11 included studies (12,774 in total in the review) • Diagnosed CAP	Shorter-duration antibiotic treatments: 5 days or less	Longer-duration antibiotic treatment, with a minimum difference of 2 days in duration of therapy	Relevant outcomes: • Clinical cure • Mortality • Invasive ventilation • ICU admission • Need for hospitalization • Duration of hospital stay • Duration of ICU stay • Severe adverse events • All adverse events. • Hospital readmission Outcomes not included: • Treatment failure • Relapse • Need for change in antibiotics	Low risk of bias Directly applicable

CAP=community acquired pneumonia; ICU=intensive care unit

Table 3: Summary of studies included in Gao (2023) and updated study included from the search

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

Study details	Population	Condition	Intervention	Comparison	Outcomes (RoB)
Agarwal 2004[a] RCT India	Total N=2188 62.2% male Age range: 2-59 months Mean age: 1.4 years	Non-severe CAP Outpatients	**3 days:** Oral amoxicillin 125 mg per day thrice daily. Effective dose varied from 31 to 54 mg/kg per day	**5 days:** Oral amoxicillin 125 mg per day thrice daily. Effective dose varied from 31 to 54 mg/kg per day	• Clinical cure (high) • Mortality (low) • Need for hospitalization (some concerns) • Severe adverse events (some concerns)
Awasthi 2008 Cluster RCT India	Total N=272* 5% male 5.9 Age range: 2-59 months Mean age: 1.9 years	Non-severe pneumonia Outpatients	**3 days:** Oral amoxycillin (125 mg per tablet) thrice daily	**5 days:** Oral cotrimoxazole (20 mg trimethoprim per tablet) twice daily	• Mortality (low) • Need for hospitalization (high) • All adverse events (high)
Bielicki 2021 RCT UK and Ireland	Total N=824 51.7% male Age range: 6 months – 8.8 years Mean age: 2.3 years	Mixed severity CAP Outpatients and inpatients	**3 days:** Low-dose: oral amoxicillin 35–50 mg/kg per day split between 2 doses High-dose: oral amoxicillin 70–90 mg/kg per day twice daily	**7 days:** Low-dose: oral amoxicillin 35–50 mg/kg per day twice daily High-dose: oral amoxicillin 70–90 mg/kg per day twice daily	• Mortality (low) • Severe adverse events (low)
Ginsburg 2020 RCT Malawi	Total N= 3000 55.1% male	Non-severe Outpatients	**3 days:** Oral amoxicillin twice daily (2 to 11 months: 500 mg per day, 12 to 35 months:	**5 days:** Oral amoxicillin twice daily (2 to 11 months: 500 mg per day, 12 to 35 months:	• Mortality (low) • Severe adverse events (low)

Study details	Population	Condition	Intervention	Comparison	Outcomes (RoB)
	Age range: 2-59 months		1000 mg per day, 36 to 59 months: 1500 mg per day)	1000 mg per day, 36 to 59 months: 1500 mg per day)	
Gomez Campdera 1996 RCT Spain	Total N=155 59.3% male Age range: 6-59 months Mean age: 4.3 years	Pneumonia Outpatients	**3 days:** Oral azithromycin 10 mg/kg per day once daily	**10 days:** Under 5 y: oral amoxicillin/ clavulanic acid 40 mg/kg per day thrice daily Older than 5 y: erythromycin 40 mg/ kg per day thrice daily	• Clinical cure (high) • Need for hospitalization (high) • All adverse events (high)
Kogan 2003 RCT Chile	Total N=106 50 % male Age range: 1 month – 14 years Mean age: 5 years	Non-severe CAP Outpatients and inpatients	**3 days:** Oral azithromycin 10 mg/kg once daily	**7 days:** Classic pneumonia: oral amoxicillin 75 mg/kg per day in 3 divided doses **14 days:** atypical pneumonia: oral erythromycin 50 mg/kg per day in 3 divided doses	• All adverse events (high)
MASCOT 2002 RCT Pakistan	Total N=200 62.7% male Age range: 2-59 months Mean age: 0.9 years	Non-severe CAP Outpatients	**3 days:** Oral amoxicillin 15 mg/kg thrice daily	**5 days:** Oral amoxicillin 15 mg/ kg thrice daily	• Clinical cure (low) • Mortality (low)
Pernica 2021 RCT	Total N=281 56.9% male	CAP Outpatients	**3 days:** Oral amoxicillin 90 mg/ kg per day thrice daily	**10 days:** Oral amoxicillin 90 mg/kg per day thrice daily	• Clinical cure (low) • Severe adverse events (low)

Study details	Population	Condition	Intervention	Comparison	Outcomes (RoB)
Canada	Age range: 6 months – 10 years Mean age: 2.6 years				
Ronchetti 1994 RCT Italy	Total N=110 51.8% male Mean age: 5.3 years	Pneumonia	**3 days:** Oral azithromycin 10 mg/kg once daily	**7 days:** Oral josamycin 50 mg/ kg thrice daily	• Clinical cure (high) • All adverse events (high)
Roord 1996 RCT Netherlands	Total N=85 58.8% male Age range: 2-16 years Mean age: 5.2 years	Non-severe CAP Outpatients	**3 days:** Oral azithromycin suspension 10 mg/kg to a maximum of 500 mg per day once daily	**10 days:** Oral erythromycin suspension 40 mg/kg per day divided in three daily doses	• Clinical cure (high) • All adverse events (high)
Sadruddin 2019 Cluster RCT Pakistan	Total N=603* 53% male Age range: 2-59 months Mean age: 1.7 years	Non-severe pneumonia Outpatients	**3 days:** Oral amoxicillin suspension 50 mg/kg per day twice daily	**5 days:** Oral cotrimoxazole 40 mg sulphamethoxazole/ 8 mg trimethoprim/ kg per day (200 mg sulphamethoxazole/ 40 mg trimethoprim/ 5 mL) twice daily	• Mortality (low) • All adverse events (high) • Severe adverse events (high)

CAP=community acquired pneumonia; RCT=randomised controlled trial

*Sample size after adjusting the design effect

[a]Agarwal 2004 is referred to under this name by Gao 2023, but is published under the name Awasthi et al. 2004

See Appendix D for full evidence tables.

1.1.6 Summary of the effectiveness evidence

This information is taken from the Gao (2023) review and has been updated by NICE.

Table 4: GRADE evidence summary for short courses of antibiotics (3-5 days) vs longer courses of antibiotics (>5 days)

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with long	Risk difference with Short
Clinical cure	4361 (5 RCTs[g,m,k,p,o])	⊕◯◯◯ Very low[a,b,c]	**OR 1.13** (0.80 to 1.60)	875 per 1,000	**13 more per 1,000** (27 fewer to 43 more)
Clinical cure - 3 vs 5 days	4012 (2 RCTs[g,m])	⊕◯◯◯ Very low[a,c]	**OR 0.88** (0.72 to 1.08)	897 per 1,000	**12 fewer per 1,000** (34 fewer to 7 more)
Clinical cure - 3 vs 10 days	239 (2 RCTs[k,p])	⊕◯◯◯ Very low[a,c]	**OR 1.66** (0.97 to 2.82)	566 per 1,000	**118 more per 1,000** (7 fewer to 220 more)
Clinical cure - 3 vs 7 days	110 (1 RCT[o])	⊕◯◯◯ Very low[a,c]	**OR 2.01** (0.86 to 4.70)	644 per 1,000	**140 more per 1,000** (35 fewer to 250 more)
Mortality	8587 (6 RCTs[g,h,j,m,q,i])	⊕⊕⊕⊕ High	not estimable[r]	1 per 1,000	**1 fewer per 1,000** (1 fewer to 1 fewer)
Mortality - 3 vs 5 days	7773 (5 RCTs[g,h,j,m,q])	⊕⊕⊕⊕ High	not estimable[r]	1 per 1,000	**1 fewer per 1,000** (1 fewer to 1 fewer)

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with long	Risk difference with Short
Mortality - 3 vs 7 days	814 (1 RCT[i])	⨁⨁⨁⨁ High	not estimable[r]	0 per 1,000	**0 fewer per 1,000** (0 fewer to 0 fewer)
Need for hospitalisation	2478 (3 RCTs[g,h,k])	⨁⨁◯◯ Low[a]	not estimable[r]	21 per 1,000	**21 fewer per 1,000** (21 fewer to 21 fewer)
Need for hospitalisation - 3 vs 5 days	2323 (2 RCTs[g,h])	⨁⨁◯◯ Low[a]	not estimable[r]	20 per 1,000	**20 fewer per 1,000** (20 fewer to 20 fewer)
Need for hospitalisation - 3 vs 10 days	155 (1 RCT[k])	⨁⨁◯◯ Low[a]	not estimable[r]	41 per 1,000	**41 fewer per 1,000** (41 fewer to 41 fewer)
Serious adverse events	6472 (4 RCTs[g,j,q,i])	⨁◯◯◯ Very low[a,d]	not estimable[r]	47 per 1,000	**47 fewer per 1,000** (47 fewer to 47 fewer)
Serious adverse events - 3 vs 5 days	5658 (3 RCTs[g,j,q])	⨁◯◯◯ Very low[a,d]	not estimable[r]	48 per 1,000	**48 fewer per 1,000** (48 fewer to 48 fewer)
Serious adverse events - 3 vs 7 days	814 (1 RCT[i])	⨁⨁⨁⨁ High	not estimable[r]	45 per 1,000	**45 fewer per 1,000** (45 fewer to 45 fewer)
All adverse events	1266 (6 RCTs[h,q,o,k,p,l])	⨁◯◯◯ Very low[a,e]	**RR 1.13** (0.60 to 2.14)	52 per 1,000	**7 more per 1,000** (21 fewer to 59 more)

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with long	Risk difference with Short
All adverse events - 3 vs 5 days	863 (2 RCTs[h,q])	⊕◯◯◯ Very low[a,c]	**RR 2.26** (0.82 to 6.21)	13 per 1,000	**17 more per 1,000** (2 fewer to 69 more)
All adverse events - 3 vs 7 days	110 (1 RCT[o])	⊕◯◯◯ Very low[a,e]	**RR 0.69** (0.15 to 3.28)	67 per 1,000	**21 fewer per 1,000** (57 fewer to 152 more)
All adverse events - 3 vs 10 days	234 (2 RCTs[k,p])	⊕◯◯◯ Very low[a,e,f]	**RR 1.07** (0.40 to 2.91)	164 per 1,000	**11 more per 1,000** (98 fewer to 313 more)
All adverse events - 3 vs 14 days	59 (1 RCT[l])	⊕◯◯◯ Very low[a,e]	**RR 0.11** (0.01 to 2.10)	115 per 1,000	**103 fewer per 1,000** (114 fewer to 127 more)
All adverse events subgroup analysis by age group	863 (2 RCTs[h,q])	⊕◯◯◯ Very low[a,c]	**RR 2.26** (0.82 to 6.21)	13 per 1,000	**17 more per 1,000** (2 fewer to 69 more)
All adverse events subgroup analysis by age group - < 5 years	863 (2 RCTs[h,q])	⊕◯◯◯ Very low[a,c]	**RR 2.26** (0.82 to 6.21)	13 per 1,000	**17 more per 1,000** (2 fewer to 69 more)
Clinical Cure subgroup analysis by age group	4263 (3 RCTs[g,m,n,])	⊕◯◯◯ Very low[a,c]	**OR 0.90** (0.67 to 1.19)	894 per 1,000	**10 fewer per 1,000** (44 fewer to 15 more)
Clinical Cure subgroup analysis by age group - < 5 years	4201 (3 RCTs[g,m,n])	⊕◯◯◯ Very low[a,c]	**OR 0.92** (0.72 to 1.19)	895 per 1,000	**8 fewer per 1,000** (35 fewer to 15 more)

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with long	Risk difference with Short
Clinical Cure subgroup analysis by age group - 5 to 18 years	62 (1 RCT[n])	⊕⊕◯◯ Low[e]	**OR 0.40** (0.11 to 1.39)	857 per 1,000	**151 fewer per 1,000** (460 fewer to 36 more)
Mortality subgroup analysis by severity of CAP	8587 (7 RCTs[g,h,l,j,m,q])	⊕⊕⊕⊕ High	not estimable[r]	1 per 1,000	**1 fewer per 1,000** (1 fewer to 1 fewer)
Mortality subgroup analysis by severity of CAP - None-severe pneumonia	8219 (6 RCTs[g,h,l,j,m,q])	⊕⊕⊕⊕ High	not estimable[r]	1 per 1,000	**1 fewer per 1,000** (1 fewer to 1 fewer)
Mortality subgroup analysis by severity of CAP - Severe pneumonia	368 (1 RCT[i])	⊕⊕⊕⊕ High	not estimable[r]	0 per 1,000	**0 fewer per 1,000** (0 fewer to 0 fewer)

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

a. Downgraded twice for risk of bias due to inadequate allocation concealment and lack of blinding (rated by Gao 2023)
b. Downgraded once as I2 was between 33.3% and 66.7% (I2 = 54%)
c. 95% CI crosses 1 MID (0.8 or 1.25)
d. Downgraded twice as I2 was over 66.8% (I2 = 94%)
e. 95% CI crosses 2 MIDs (0.8 and 1.25)

f. Downgraded once as I2 was between 33.3% and 66.7% (I2 = 64%)
g. Agarwal 2004
h. Awasthi 2008
i. Bielicki 2021
j. Ginsburg 2020
k. Gomez Campdera 1996
l. Kogan 2003
m. MASCOT 2002
n. Pernica 2021
o. Ronchetti 1994
p. Roord 1996
q. Sadruddin 2019
r. Relative effect was not estimable as risk difference provides an absolute effect only

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. Leaving no included studies for this review question. 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

There are no included studies in this review question.

1.1.9 Economic model

No original economic modelling was completed for this review question.

1.1.10 Unit costs

No unit costs were supplied for this review question.

1.1.11 References – included studies

1.1.11.1 Effectiveness

Awasthi, S Agarwal, G Singh, JV Kabra, SK Pillai, RM Singhi, S Nongkynrih, B Dwivedi, R More, VB Kulkarni, M Niswade, AK Bharti, B Ambast, A Dhasmana, P (2008) Effectiveness of 3-Day Amoxycillin vs. 5-Day Co-trimoxazole in the Treatment of Non-severe Pneumonia in Children Aged 259 Months of Age: A Multi-centric Open Labeled Trial. JOURNAL OF TROPICAL PEDIATRICS 54(6): 382 - 389

Awasthi, S Kabra, SK Kulkarni, M Murali, N Niswade, AK Pillai, RM Singhi, S Chande, CA Das, B Jain, A Kamath, J Mathur, M Raje, K Roy, P Lalitha, MK Agarwal, G Jayseelan, L Qazi, S Agarwal, G Awasthi, S Kabra, SK Kaul, A Singhi, S Walter, SD Pande, JN Wakhlu, I (2004) Three day versus five day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomised controlled trial. BMJ-BRITISH MEDICAL JOURNAL 328(7443): 791 - 794

Bielicki, JA Stöhr, W Barratt, S Dunn, D Naufal, N Roland, D Sturgeon, K Finn, A Rodriguez-Ruiz, JP Malhotra-Kumar, S Powell, C Faust, SN Alcock, AE Hall, D Robinson, G Hawcutt, DB Lyttle, MD Gibb, DM Sharland, M (2021) Effect of Amoxicillin Dose and Treatment Duration on the Need for Antibiotic Re-treatment in Children With Community-Acquired Pneumonia The CAP-IT Randomized Clinical Trial. JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 326(17): 1713 - 1724

Gao, Ya, Liu, Ming, Yang, Kelu et al. (2023) Shorter Versus Longer-term Antibiotic Treatments for Community-Acquired Pneumonia in Children: A Meta-analysis. Pediatrics 151(6)

Ginsburg, AS Mvalo, T Nkwopara, E McCollum, ED Phiri, M Schmicker, R Hwang, J Ndamala, CB Phiri, A Lufesi, N May, S (2020) Amoxicillin for 3 or 5 Days for Chest-Indrawing Pneumonia in Malawian Children. NEW ENGLAND JOURNAL OF MEDICINE 383(1): 13 - 23

Gomez Campdera, J.A., Navarro Gomez, M.L., Hernandez-Sampelayo, T. et al. (1996) Azithromycin in the treatment of ambulatory pneumonia in children. Acta Pediatrica Espanola 54(8): 554-562

Hazir, T Latif, E Qazi, SA Rafi, M Latif, E Ansari, S Farouki, S Murtaza, A Munir, S Maqbool, S Randhawa, S Iqbal, I Riaz, S Kundi, Z Aslam, S Asghar, R Hazir, T Latif, E Ansari, S Farouki, S Bin Nisar, Y Munir, S Iqbal, I Asghar, R Aslam, S Qazi, SA Bari, A (2002) Clinical efficacy of 3 days versus 5 days of oral amoxicillin for treatment of childhood pneumonia: a multicentre double-blind trial. LANCET 360(9336): 835 - 841

Kogan, R Martínez, MA Rubilar, L Payá, E Quevedo, I Puppo, H Girardi, G Castro-Rodriguez, JA (2003) Comparative randomized trial of azithromycin versus erythromycin and amoxicillin for treatment of community-acquired pneumonia in children. PEDIATRIC PULMONOLOGY 35(2): 91 - 98

Pernica, JM Harman, S Kam, AJ Carciumaru, R Vanniyasingam, T Crawford, T Dalgleish, D Khan, S Slinger, RS Fulford, M Main, C Smieja, M Thabane, L Loeb, M (2021) Short-Course Antimicrobial Therapy for Pediatric Community-Acquired Pneumonia The SAFER Randomized Clinical Trial. JAMA PEDIATRICS 175(5): 475 - 482

Ronchetti, R Blasi, F Grossi, E Pecori, A Bergonzi, F Ugazio, A Giovannini, M Crua, C Corda, R Delia, G Imperato, C Morgese, G Bartolotta, E Baldini, G Lagrutta, A Impallomeni, Mr Russo, G Campagna, A Corvaglia, E Schettini, F Delgiudice, MM Bini, G Villa, MP (1994) The role of azithromycin in treating children with community-acquired pneumonia. CURRENT THERAPEUTIC RESEARCH-CLINICAL AND EXPERIMENTAL 55(8): 965 - 970

Roord, JJ Wolf, BHM Goossens, MMHT Kimpen, JLL (1996) Prospective open randomized study comparing efficacies and safeties of a 3-day course of azithromycin and a 10-day course of erythromycin in children with community-acquired acute lower respiratory tract infections. ANTIMICROBIAL AGENTS AND CHEMOTHERAPY 40(12): 2765 - 2768

Sadruddin, S Khan, IU Fox, MP Bari, A Khan, A Thea, DM Khan, A Khan, I Ahmad, I Qazi, SA (2019) Comparison of 3 Days Amoxicillin Versus 5 Days Co-Trimoxazole for Treatment of Fast-breathing Pneumonia by Community Health Workers in Children Aged 2-59 Months in Pakistan: A Cluster-randomized Trial. CLINICAL INFECTIOUS DISEASES 69(3): 397 - 404

1.1.11.2 Economic

No economic studies were included

1.1.12 The committee's discussion and interpretation of the evidence

1.1.13.1. The outcomes that matter most

The committee agreed that although mortality was the key outcome, it was quite rare for a baby, child or young person (BCYP) to die from community-acquired pneumonia (CAP) in high income countries (HIC), so therefore they would expect the number of events to be low. Bearing this in mind they agreed that other outcomes such as need for hospitalisation, clinical cure and the number of adverse events would be important for decision making. The committee agreed that, even though it is not an outcome that can be measured easily in studies, the aim of considering length of antibiotic courses in BCYP is to improve antimicrobial stewardship.

1.1.13.2 The quality of the evidence

The committee discussed a systematic review and meta-analysis by Gao et al (2023). They discussed that the PICO of the systematic review defined shorter treatment durations as 5 days or less while the PICO for this review defined shorter treatment durations as less than 5 days. Therefore, comparisons from the Gao et al (2023) review in which a course of 5 days was categorised as a short duration were removed from the analysis. The update search did not identify any further evidence published since the publication of this systematic review.

The committee further noted that the Gao review was assessed to be at low risk of bias.

The committee noted that the included 11 studies from the Gao review were conducted all over the world, including in low and middle income countries (LMIC), and discussed whether this might have an impact on the applicability of the studies to the UK, however, a sub-group analysis undertaken by Gao et al found that for the outcomes of interest there was no meaningful heterogeneity between LMIC and HIC sub-groups. The committee further noted that there was variation in the inclusion criteria in the included studies, for example some excluded people with underlying chronic disease, or complicated pneumonia. They discussed the study done in the UK which they considered to be key to the decision-making in the area. While this study does include a relevant pneumonia population, it does not include those with complicated pneumonia and the committee agreed that any recommendations will need to clearly be for those with non-severe pneumonia. Those with severe disease will need to remain prescribed 5 days of antibiotics.

The committee noted that there were some discrepancies between the evidence and usual practice in the UK. The key ones for their consideration were antibiotic choice and duration of treatment for the comparisons. They agreed that the standard of care in the UK was a 5-day course of antibiotics, so therefore the comparator they were most interested in was 3 days vs 5 days. Comparisons of 3 vs 7 days and 3 vs 10 days, were less useful because babies, children and young people in the UK would not normally have antibiotics for so long. They noted the only UK study in the systematic review compared 3 days with 7 days of amoxicillin. In terms of antibiotic choice, the committee noted that the standard of care as set out in the existing NICE recommendations are amoxicillin for non-severe symptoms and co-amoxiclav for severe symptoms. In the 5 included studies that compared 3 to 5 days, all of the

studies used amoxicillin in their intervention group. The committee agreed that this was a good match. Studies using azithromycin were considered by the committee to be less applicable as the usual course for azithromycin is 3 days, not 5 days as has been usual practice for other antibiotics. The subgroup for 3 days compared with 5 days did not include studies of azithromycin and was consistent with pooled findings from all durations in identifying no differences between the shorter and longer duration courses. GRADE was used to assess the confidence in the findings of the meta-analyses; for most of the outcomes of interest, the evidence was found to give moderate confidence in the pooled effect estimate, for mortality the confidence was high, and for a composite of all adverse events confidence was low. Overall, the strength of the evidence, combined with the committee's expertise and experience allowed them to make strong recommendations about antibiotic duration for babies and children, however they noted that for young people the evidence was much sparser, with the majority of the studies focussing on babies and children, therefore they did not make a recommendation for young people aged 11-18.

6 studies did not use the same antibiotic in the intervention and comparison arms, which made it difficult to determine whether the differences found were the result of the different durations. Of these, 4 studies (Gomez Campdera 1996, Kogan 2003, Ronchetti 1994, and Roord 1996) used azithromycin as the shorter course. The committee decided that these studies were less applicable as azithromycin is not used in the UK. The other 2 studies (Awasthi 2008 and Sadruddin 2019) used a combination of antibiotics that the committee were satisfied reflected common UK prescribing, so they did not consider the difference in antibiotic choice between study arms to reduce the validity of these 2 studies.

1.1.13.3 Benefits and harms

The committee agreed that for the most important outcomes, clinical cure, hospitalisation, adverse events and severe adverse events, and for mortality, there was no difference between 3 days and 5 days of antibiotics. This was also true of the other durations of antibiotics.

Further, they noted that although the subgroup analyses that showed that, for mortality there were no differences identified between the groups, the event numbers were few, with many studies reporting no mortality in either intervention or control group. Overall adverse effects findings did not show a difference between the shorter and longer antibiotic courses. Sub-group analysis for clinical cure as well as adverse events also found that the effectiveness of the antibiotics did not vary by age group.

The data reassured the committee that for babies and children, there were no negative consequences to prescribing a 3-day course of antibiotics instead of the standard 5-day course, and in addition this represented better antimicrobial stewardship. They noted that there were circumstances where a longer course might be appropriate, for example if the baby or child was not improving as expected.

The committee further discussed the ages of the children included in the studies; they noted the mean ages ranged from around 1 to just over 5 years, with children up to 11 included in some studies. While they agreed that this restricted the recommendations that could be made, they nonetheless also agreed that recommendations could be made for children up to 11 years. The committee further discussed the lower age and agreed that babies under 3 months are treated

differently to children above this age due to the development of their immune systems and the types of infections they are prone to. Therefore the committee expressed that they would have concerns about reducing the duration of antibiotics and agreed to keep this as 5 days for this age group.

The committee discussed the importance of managing parents' and carers' expectations of antibiotics for their child. They agreed that parents and carers were used to longer courses of antibiotics and might be anxious about a shorter course. The committee agreed that it was important to reassure them, and also to explain to them that their child's symptoms may not be resolved by the end of the course of antibiotics. Although their child's symptoms would not be gone, the committee agreed that safety-netting is important, and that parents and carers should understand when and how to get back in contact with services if their child's condition is worsening.

1.1.13.4 Cost effectiveness and resource use

There was no existing cost effectiveness evidence for this review question. Currently babies, children and young people are prescribed a five-day course of antibiotics. The clinical evidence showed that there was no clinical difference between three and five days. Therefore, reducing the length of antibiotic treatment should be cost saving if pack size and costs are adjusted. The committee noted there was likely to be an increase in re-consultations. However, the potential cost impact may be mitigated if healthcare practitioners explain to parents and carers that their baby's or child's symptoms may persist after stopping antibiotics. Additionally, the cost impact of increased re-consultations is likely to be negligible compared to the potential benefits of antibiotic stewardship.

1.1.13.5 Other factors the committee took into account

The committee agreed that in most cases a baby or child with suspected pneumonia in primary care would be referred to secondary or urgent care for an assessment and diagnosis, and therefore antibiotics for pneumonia would normally be prescribed in that setting. The committee agreed that shorter courses given in secondary care could help minimise the number of babies and children who are potentially overprescribed antibiotics for coughs and minor lower respiratory tract infections because of pressure from parents and carers or because of caution by primary care GPs.

The committee acknowledged that changing antibiotic duration for children with pneumonia will mean that there is a difference in what is recommended in this guideline and what is recommended elsewhere in NICE guidance for children with non-pneumonia respiratory tract infections. While they did agree that this could potentially create uncertainty and that there may be implementation impacts, the committee nonetheless agreed that the evidence did support the 3-day duration recommendation.

Appendices

Appendix A – Review protocols

Review title	The clinical and cost-effectiveness of shorter durations of antibiotic treatment compared to longer antibiotic treatment courses for babies, children and young people with community-acquired pneumonia.
Review question	Are shorter durations of antibiotic treatment effective and cost-effective at treating babies, children and young people with community-acquired pneumonia compared to longer treatment courses?
Objective	To compare the clinical and cost effectiveness of short courses of antibiotics (<5 days) and longer courses of antibiotics (≥ 5 days) for babies, children and young people (<18 years) with community-acquired pneumonia.
Searches	**Overall approach** The searches will comprise the following elements: • a combined search for cost effectiveness evidence covering all review questions in this guideline. • a combined search for systematic reviews covering all review questions in this guideline. • searches for effectiveness evidence to update the Gao et al. (2023) review. **Searches for cost effectiveness evidence** A combined search will be undertaken to cover the cost effectiveness aspects of all the review questions in a single search.

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

	• Epistemonikos via https://www.epistemonikos.org/ This is the standard NICE practice agreed by the Guidelines Methods Group in September 2022 for identifying systematic reviews for routine guideline searches. **Effectiveness evidence: searches specific to this review question** The searches for effectiveness evidence will update the searches done for Gao et al. (2023). These searches were run on 30 April 2022. The update search will use the same databases as Gao et al.: • Cochrane Central Register of Controlled Trials (CENTRAL) via Wiley • Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCOhost • Embase via Ovid • MEDLINE ALL via Ovid The same study-type filters will be applied as Gao et al. to identify randomised controlled trials. The same limits will also be applied, with the addition of a date limit for April 2022 to current. To ensure potentially relevant records are not missed any later citations of Gao et al. will be identified. The guideline committee or other stakeholders could also be asked if they are aware of any other potentially relevant studies that could be considered.

	Managing all search results Database functionality will be used, where available, to exclude from all searches: • Animal studies • Conference abstracts and posters • Editorials, letters, news items and commentaries • Registry entries for ongoing clinical trials or those that contain no results • Theses and dissertations • Papers not published in the English language With the agreement of the guideline committee, the searches will be re-run 6-8 weeks before final submission of the review and further studies retrieved for inclusion. The information services team at NICE will quality assure the principal search strategy and peer review the other strategies. Any revisions or additional steps will be agreed by the review team before being implemented. The full search strategies for all databases will be published in the final review.
Condition or domain being studied	Community acquired pneumonia
Population	Inclusion: • Babies over 28 days (corrected gestational age), children and young people (age <18 years) with community acquired pneumonia. • CAP is defined as pneumonia that is acquired outside hospital.

	Exclusion: • Babies up to and including 28 days (corrected gestational age). • People with COVID-19 pneumonia. • People who acquire pneumonia while intubated (ventilator-associated pneumonia). • People who are severely immune-compromised (have a primary immune deficiency or secondary immune deficiency related to HIV infection, or severe drug or systemic disease-induced immunosuppression, for example, people who have taken immunosuppressant cancer therapy or undergone organ transplantation). • People in whom pneumonia is an expected terminal event. • People with non-pneumonic infective exacerbations of bronchiectasis. • People with non-pneumonic infective exacerbations of chronic obstructive pulmonary disease. • People with pneumonia associated with cystic fibrosis. • People with aspiration pneumonia as a result of inhaling a large bolus of gastric contents.
Intervention	**Shorter duration of treatment (<5 days)** Antibiotic treatment for CAP – any of the below alone or in combination: • macrolides (including ketolides)

	• beta-lactams (cephalosporins and penicillins), subdivided into:
	  ○ narrow-spectrum beta-lactams:
	  ▪ class 1: penicillin G (benzylpenicillin), phenoxymethylpenicillin (penicillin V)
	  ▪ class 2: ampicillin, amoxicillin
	  ○ broad-spectrum beta-lactams:
	  ▪ beta-lactamase stable penicillins: co-amoxiclav, piperacillin-tazobactam, timentin (ticarcillin-clavulanic acid), flucloxacillin, co-fluampicil
	  ▪ cephalosporins
	• tetracyclines
	• respiratory fluoroquinolones.
	Route of administration may be intravenous or oral.
	Note: only UK-licensed interventions and standard dose ranges will be considered.

Comparator	**Longer duration of treatment (≥5 days)** • Any agent from the above classes compared for different durations (i.e. different durations of the same antibiotic or different antibiotics within a class). **Note**: studies that switch from intravenous to oral will be included and the duration of interest will be the full treatment duration (intravenous + oral).
Types of study to be included	Systematic reviews of RCTs and RCTs
Other exclusion criteria	Studies using biomarkers to allow targeted shortening of treatment will be excluded.

	Studies investigating hospital-acquired pneumonia will be excluded. Studies where the proportion of ineligible patients (e.g. 18 years or older; patients with HAP) was more than 20% will be excluded.
Context	The NICE guideline on pneumonia in adults was withdrawn (May 2020) during the COVID-19 pandemic. At that time, COVID-19 pneumonia was the prevalent form of pneumonia in the UK and there were concerns that CG191 was diverting healthcare professionals away from NICE's COVID-19 rapid guideline on pneumonia in adults in the community (now replaced by COVID-19 rapid guideline: managing COVID-19). There was also potential for confusion among guideline users by having 2 NICE guidelines on pneumonia in adults that covered similar topic areas but had different recommendations (NG138 pneumonia (community-acquired): antimicrobial prescribing; and NG139 pneumonia (hospital-acquired): antimicrobial prescribing). Additionally, some recommendations in NICE guideline CG191 were not suitable in the context of the pandemic. The pandemic situation has evolved, and the guideline now needs to be reinstated. However, an update to the guideline is also needed to reflect changes in pneumonia management brought about by COVID-19, and to address the potential impact of this update on 3 other related NICE guidelines, to ensure NICE has cohesive guidelines on COVID and non-COVID pneumonia.

	The proposed update will focus on amending recommendations in light of the COVID-19 pandemic, and ensuring this guideline aligns with other NICE guidance on COVID and non-COVID pneumonia.
Primary outcomes (critical outcomes)	• Mortality at any time point • Need for invasive ventilation (in those not requiring invasive ventilation at baseline) • ICU admission (in those not requiring ICU admission at baseline) • Hospital admission and duration of hospital stay • Clinical cure at the end of follow up.

Secondary outcomes (important outcomes)	By end of follow-up
	• HRQoL (measured by CAP symptom questionnaire, EQ5D, or SF-36).
	• Treatment-related adverse events, including:
	  ○ Gastrointestinal bleeding
	  ○ Hyperglycaemia
	  ○ Complications (composite of empyema, effusion, abscess, metastatic infection, superinfection, MODS)
	  ○ Withdrawal due to treatment-related adverse events

Data extraction (selection and coding)	For new papers identified from the search: All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.

	The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. Any disagreements will be resolved by discussion with other members of the technical review team. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow. The priority screening functionality within the EPPI-reviewer software will not be used for this review.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For SRs (including the Gao 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	Data from the Gao 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. For any additional papers identified from the 'top up' search, results from the individual studies will be compared to those in the Gao review and depending on the level of agreement, a decision will be made whether to report individual study results in addition to

	the review findings (as further supporting evidence in line with Gao results), or whether to incorporate the new results into the analyses reported in Gao and present them as new analyses (where the new evidence is not supportive of Gao results and needs to be combined).
Analysis of sub-groups	The following groups will be considered separately if data are available: • Severity of CAP* • Age range: Age: 0-1 (infants); 1-5 (pre-school age children); 5-18 (school age children). • Specific antibiotic durations: 3 vs 5 days; 3 vs 7 days; 3 vs 10 days; 5 vs 10 days. • Pathogen type *Severity status will be defined by formal severity assessment tools (such as PSI or CURB65) where possible. Place of management will be used as a surrogate of severity assessment where formal assessment using tools is not provided. Patients with CAP managed as outpatients will be considered as having low-severity CAP, and patients with CAP managed in hospital/ICU will be considered as having high-severity CAP.
Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)

Language	English
Country	England

1

2

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. This was used to identify a review by Gao et al. (2023).

Gao Y et al. (2023) Shorter Versus Longer-term Antibiotic Treatments for Community-Acquired Pneumonia in Children: A Meta-analysis. *Pediatrics*, 151(6), e2022060097. https://doi.org/10.1542/peds.2022-060097

- Part 2: Effectiveness evidence searches

This searches for Gao et al. (2023) were done on 30 April 2022. This update of those searches was done on 4 April 2024 and re-run on 17 October 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 for Part 1 and Part 3 were quality assured (QA) by a trained NICE SIS. The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage. All translated search strategies were peer reviewed by another SIS to ensure their accuracy. All QA procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

The Gao et al. (2023) searches were quality assured by a NICE SIS and minor amendments were made to the update searches, as described below.

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 exclusively set in countries that are not members of the Organisation for Economic Co-operation and Development (OECD), in line with the search protocol. The filters were used without amendment. The filters are not available for the other databases used.

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

The Effectiveness (Part 2) update searches used the same limits and filters as Gao et al. (2023).

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 (Part 2) update searches used a date limit of 20 April 2022-current in order to update the Gao et al. (2023) searches, which were conducted on 30 April 2022.

Study-type filters

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

The Effectiveness (Part 2) update searches used the same filters to retrieve randomised controlled trials as Gao et al. (2023).

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 and 3: Pneumonia terms

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

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

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

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

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

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

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

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

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

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

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

Part 2: Effectiveness evidence searches

This is a re-run of the searches done for Gao et al. (2023). The searches in the supplementary materials attached to the final version of Gao et al. (2023) do not exactly match the versions contained in the preprint of the same article. The preprint version was used as the final article version contained formatting issues and part of the CINAHL search was missing.

The searches were run to be consistent with Gao et al. and not with other searches for this guideline. Therefore, the Gao et al. approaches to pneumonia, children, study filters and limits were adopted.

No changes were made where the Gao et al. searches could have been shortened e.g. in Embase exp antibiotic agent/ was retained on Line 13, although it was already covered by exp antiinfective agent/ on Line 12.

The Gao et al. searches in CENTRAL were conducted in the Ovid version but this update was done in Wiley. The only change was to switch the free-text lines from the .mp field to the :ti,ab,kw fields.

Gao et al. did their searches on 30 April 2022. These searches were run from 20 April 2022-current, giving a week's overlap to make sure no studies were missed.

There are some minor differences between the appearance of some lines in CINAHL between the searches below and those reported in Gao et al. These do not affect the results and are from the way that the terms were entered and automatically reformatted by the interface (e.g. the subject headings were added using the thesaurus, rather than by pasting directly from Gao et al.). It was not clear why Gao et al. had deviated from MEDLINE by including the word school on S55 when different types of school had been included on S54 but this broader approach was retained for consistency.

There seemed to be an error in the way that some of the antibiotics had been formatted in Gao et al. There are no drugs called ceQriaxone, ceQibuten, celriaxone or celrioxone. These seemed to be errors for the antibiotics ceftriaxone, ceftrioxone and ceftibuten. These names were added to all of the strategies. The strategies were re-run without date limits to verify that Gao et al. had not missed any potentially relevant studies by omitting these named antibiotics. No additional studies were identified, which is probably because Gao et al. had already included the correct subject headings.

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

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

Searches
#3 #1 or #2 16754
#4 #1 or #2 in Cochrane Reviews 244
#5 #1 or #2 with Cochrane Library publication date Between Jan 2014 and Nov 2023, in Cochrane Reviews 177
Note: in the re-run Line #5 was changed to #1 or #2 with Cochrane Library publication date Between Nov 2023 and Oct 2024, in Cochrane Reviews.

Database name: Epistemonikos

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

Searches

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

This is the final search as formatted by Epistemonikos:

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

Results:

Total: 48055

Apply Publication Year limits of 2014-2024: 30820

Download 1: Apply Publication type - Systematic Review: 2307

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

Part 2: Effectiveness evidence searches to update Gao et al. (2023)

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	4/4/2024	Wiley	Cochrane Central Register of Controlled Trials Issue 3 of 12, March 2024	42
Cumulative Index to Nursing and Allied Health Literature (CINAHL)	4/4/2024	EBSCOhost	1981-Current	9
Embase	4/4/2024	Ovid	Embase 1974 to 2024 April 03	141
MEDLINE ALL	4/4/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to April 03, 2024	125

Additional search techniques

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Forward citation searching	4/4/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-04-01	1
Forward citation searching update	17/10/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-10-15	3
Reference list checking	4/4/2024	Web of Science (WOS) Core Collection (1990-present)	Data updated 2024-04-01	16

Re-run results

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	17
Cumulative Index to Nursing and Allied Health Literature (CINAHL)	17/10/2024	EBSCOhost	1981-Current	1
Embase	17/10/2024	Ovid	Embase 1974 to 2024 October 16	41
MEDLINE ALL	17/10/2024	Ovid	Ovid MEDLINE(R) ALL 1946 to October 16, 2024	40

Search strategy history

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

Searches		
#1	(communit* NEAR/5 pneumon*):ti,ab,kw	1904
#2	cap:ti,ab,kw	5559
#3	[mh ^"community-acquired infections"]	776
#4	(community-acquired or community acquired):ti,ab,kw	3059
#5	#3 or #4	3059
#6	[mh Pneumonia]	12533
#7	(pneumon* or bronchopneumon* or pleuropneumon*):ti,ab,kw	25963
#8	#6 or #7	32631
#9	#5 and #8	1980
#10	#1 or #2 or #9	6859
#11	[mh "Anti-Bacterial Agents"]	16856
#12	(anti-biotic* or antibiotic*):ti,ab,kw	38424
#13	[mh Macrolides]	12062
#14	[mh "beta-Lactams"]	11530
#15	[mh Quinolones]	6273
#16	[mh Tetracyclines]	3083
#17	(amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or celriaxone* or	

Searches
cefuroxime* or cotrimoxazole* or co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or Ceftriaxone* or celrioxone* or Ceftrioxone* or cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracycline* or trimethoprim* or ketolides* or telithromycin* or clavulanic* or co-amoxiclav* or ceQriaxone* or ceQibuten* or ceftibuten* or cefpodoxime* or fluoroquinalone* or oxytetracycline* or doxycycline*):ti,ab,kw 36859
#18 {or #11-#17} 75295
#19 [mh Infant] 45994
#20 (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*):ti,ab,kw 110923
#21 [mh Child] 81699
#22 (child* or schoolchild* or school-age* or preschool* or kid or kids or toddler*):ti,ab,kw 204224
#23 [mh ^Adolescent] 136681
#24 (adoles* or teen* or boy* or girl*):ti,ab,kw 180710
#25 [mh ^Minors] 15
#26 [mh ^Puberty] 388
#27 (minor* or pubert* or pubescen*):ti,ab,kw 29186
#28 [mh Pediatrics] 1043
#29 (pediatric* or paediatric*):ti,ab,kw 45989
#30 [mh Schools] 5698
#31 (nursery-school* or kindergar* or primary-school* or secondary-school* or elementary-school* or high-school* or highschool*):ti,ab,kw 12386
#32 {or #19-#31} 410155
#33 #10 and #18 and #32 498
#34 #10 and #18 and #32 in Trials 485
Post search filter: Date added to CENTRAL trials database: 20/04/2022 to 30/04/2024 42
Note: in the re-run the Post search filter was changed to Date added to CENTRAL trials database: 01/04/2024 to 17/10/2024

Database name: Cumulative Index to Nursing and Allied Health Literature (CINAHL)

Searches		
S1	(MH "Randomized Controlled Trials")	142,940
S2	(MH "Double-Blind Studies")	54,608
S3	(MH "Single-Blind Studies")	16,202
S4	(MH "Random Assignment")	84,434
S5	(MH "Pretest-Posttest Design")	55,581
S6	(MH "Cluster Sample")	5,504
S7	TI (randomised OR randomized)	149,486
S8	AB (random*)	402,071
S9	TI (trial)	191,690
S10	MH sample size AND AB (assigned OR allocated OR control)	4,482

Searches
S11 (MH "Placebos") 14,052
S12 PT (randomized controlled trial) 156,314
S13 AB (control W5 group) 148,475
S14 MH crossover design AND MH comparative studies 5,119
S15 AB (cluster W3 RCT) 509
S16 (MH "Animals+") 102,846
S17 (MH "Animal Studies") 156,987
S18 TI (animal model*) 3,676
S19 S16 OR S17 OR S18 250,679
S20 (MH "Human") 2,785,952
S21 S19 NOT S20 216,150
S22 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 691,747
S23 S22 NOT S21 662,492
S24 (MH "Community-Acquired Pneumonia") 1,478
S25 TI communit* N5 pneumon* OR AB communit* N5 pneumon* 4,472
S26 TI CAP or AB CAP 8,539
S27 (MH "Community-Acquired Infections") 4,468
S28 TI (community acquired or community-acquired) or AB (community acquired or community-acquired) 6,415
S29 S27 or S28 8,131
S30 (MH "Pneumonia+") 33,950
S31 TI (pneumon* or bronchopneumon* or pleuropneumon*) or AB (pneumon* or bronchopneumon* or pleuropneumon*) 44,463
S32 S30 OR S31 60,573
S33 S29 AND S32 5,091
S34 S24 OR S25 OR S26 OR S33 12,742
S35 (MH "Antibiotics+") 91,018
S36 TI (anti biotic* or anti-biotic* or antibiotic*) or AB (anti biotic* or anti-biotic* or antibiotic*) 59,246
S37 (MH "Antibiotics, Macrolide+") 6,635
S38 (MH "Antibiotics, Lactam+") 14,510
S39 (MH "Antiinfective Agents, Fluoroquinolone+") 4,338
S40 (MH "Tetracyclines+") 4,434
S41 TI (amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or celriaxone* or cefuroxime* or cotrimoxazole* or co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or Ceftriaxone* or celrioxone* or Ceftrioxone* or cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracycline* or trimethoprim* or ketolides* or telithromycin* or clavulanic* or co-amoxiclav* or ceQriaxone* or ceQibuten* or ceftibuten* or cefpodoxime* or fluoroquinalone* or oxytetracycline* or doxycycline*) or AB (amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or celriaxone* or cefuroxime* or cotrimoxazole* or co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or Ceftriaxone* or celrioxone* or Ceftrioxone* or

Searches
cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracycline* or trimethoprim* or ketolides* or telithromycin* or clavulanic* or co-amoxiclav* or ceQriaxone* or ceQibuten* or ceftibuten* or cefpodoxime* or fluoroquinalone* or oxytetracycline* or doxycycline*) 29,712
S42 S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 130,445
S43 (MH "Infant+") 289,539
S44 TI (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*) OR AB (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*) 258,558
S45 (MH "Child+") 765,321
S46 TI (child* or schoolchild* or school age* or preschool* or kid or kids or toddler*) OR AB (child* or schoolchild* or school age* or preschool* or kid or kids or toddler*) 595,963
S47 (MH "Adolescence+") 613,841
S48 TI (adoles* or teen* or boy* or girl*) OR AB (adoles* or teen* or boy* or girl*) 241,241
S49 (MH "Puberty") 3,579
S50 TI (minor* or pubert* or pubescen*) OR AB (minor* or pubert* or pubescen*) 84,713
S51 (MH "Pediatrics+") 23,190
S52 TI (pediatric* or paediatric*) OR AB (pediatric* or paediatric*) 174,301
S53 MH Schools OR MH Schools, Elementary OR MH Schools, Middle OR MH Schools, Nursery OR MH Schools, Secondary OR MH Schools, Special 31,907
S54 TI (nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*) OR AB (nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*) 44,510
S55 TI school* OR AB school* 165,683
S56 S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 1,581,102
S57 S23 AND S34 AND S42 AND S56 120
S58 EM 202204* OR EM 202205* OR EM 202206* OR EM 202207* OR EM 202208* OR EM 202209* OR EM 202210* OR EM 202211* OR EM 202212* 250,178
S59 EM 2023* OR EM 2024* 314,338
S60 S58 OR S59 564,516
S61 S57 AND S60 9
Note: in the re-run the following lines were used:
S57 S23 AND S34 AND S42 AND S56
S58 EM 202404* OR EM 202405* OR EM 202406* OR EM 202407* OR EM 202408* OR EM 202409* OR EM 202410*
S59 S57 AND S58

Database name: Embase

Searches	
1	exp community acquired pneumonia/ 20547

Searches	
2	(communit* adj5 pneumon*).mp. 28631
3	cap.mp. 76385
4	exp community acquired infection/ 25139
5	(community-acquired or community acquired).mp. 42952
6	4 or 5 42952
7	exp pneumonia/ 410090
8	(pneumon* or bronchopneumon* or pleuropneumon*).mp. 570597
9	7 or 8 597816
10	6 and 9 31658
11	1 or 2 or 3 or 10 100332
12	exp antiinfective agent/ 4739163
13	exp antibiotic agent/ 1867452
14	(anti biotic* or anti-biotic* or antibiotic*).mp. 974729
15	exp macrolide/ 361295
16	exp beta lactam/ 10249
17	exp quinolone/ 6941
18	exp tetracycline derivative/ 204923
19	(amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or celriaxone* or cefuroxime* or cotrimoxazole* or co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or Ceftriaxone* or celrioxone* or Ceftrioxone* or cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracycline* or trimethoprim* or ketolides* or telithromycin* or clavulanic* or co-amoxiclav* or ceQriaxone* or ceQibuten* or ceftibuten* or cefpodoxime* or fluoroquinalone* or oxytetracycline* or doxycycline*).mp. 844220
20	or/12-19 4947907
21	exp infant/ 1164704
22	(infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*).mp. 1852916
23	exp child/ 3180138
24	(child* or schoolchild* or school age* or preschool* or kid or kids or toddler*).mp. 3293782
25	exp adolescent/ 1828389
26	(adoles* or teen* or boy* or girl*).mp. 2206351
27	"minor (person)"/ 989
28	puberty/ 31658
29	(minor* or pubert* or pubescen*).mp. 564426
30	exp pediatrics/ 129869
31	(pediatric* or paediatric*).mp. 854556
32	exp school/ 406484
33	(nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*).mp. 119062
34	or/21-33 6069705
35	Randomized controlled trial/ 815659

Searches
36 Controlled clinical study/472758
37 random$.ti,ab. 2052318
38 randomization/ 99132
39 intermethod comparison/ 305678
40 placebo.ti,ab. 375059
41 (compare or compared or comparison).ti. 621685
42 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 2896214
43 (open adj label).ti,ab. 114450
44 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 281003
45 double blind procedure/ 217596
46 parallel group$1.ti,ab. 33298
47 (crossover or cross over).ti,ab. 127617
48 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 429971
49 (assigned or allocated).ti,ab. 508103
50 (controlled adj7 (study or design or trial)).ti,ab. 467832
51 (volunteer or volunteers).ti,ab. 288119
52 human experiment/ 657267
53 trial.ti. 419895
54 or/35-53 6548072
55 (random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) 9903
56 Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.) 385943
57 (((case adj control$) and random$) not randomi?ed controlled).ti,ab. 22213
58 (Systematic review not (trial or study)).ti. 280440
59 (nonrandom$ not random$).ti,ab. 19397
60 "Random field$".ti,ab. 3058
61 (random cluster adj3 sampl$).ti,ab. 1642
62 (review.ab. and review.pt.) not trial.ti. 1183956
63 "we searched".ab. and (review.ti. or review.pt.) 52198
64 "update review".ab. 139
65 (databases adj4 searched).ab. 67121
66 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/ 1246692
67 Animal experiment/ not (human experiment/ or human/) 2620202
68 or/55-67 4496807
69 54 not 68 5769598
70 11 and 20 and 34 and 69 969
71 limit 70 to dc=20220420-20240430 141
Note: in the re-run Line 71 was changed to limit 70 to dc= 20240401-20241017.

Database name: MEDLINE ALL

Searches	
1	(communit* adj5 pneumon*).mp. 14513
2	cap.mp. 52890
3	Community-Acquired Infections/ 16194
4	(community-acquired or community acquired).mp. 28442
5	3 or 4 28442
6	exp Pneumonia/ 361304
7	(pneumon* or bronchopneumon* or pleuropneumon*).mp. 355398
8	6 or 7 566020
9	5 and 8 17798
10	1 or 2 or 9 65681
11	exp Anti-Bacterial Agents/ 834191
12	(anti biotic* or anti-biotic* or antibiotic*).mp. 480572
13	exp Macrolides/ 123610
14	exp beta-Lactams/ 141576
15	exp Quinolones/ 55142
16	exp Tetracyclines/ 53817
17	(amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or celriaxone* or cefuroxime* or cotrimoxazole* or co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or Ceftriaxone* or celrioxone* or Ceftrioxone* or cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracycline* or trimethoprim* or ketolides* or telithromycin* or clavulanic* or co-amoxiclav* or ceQriaxone* or ceQibuten* or ceftibuten* or cefpodoxime* or fluoroquinalone* or oxytetracycline* or doxycycline*).mp. 430087
18	or/11-17 1201915
19	exp Infant/ 1270839
20	(infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*).mp. 1829095
21	exp Child/ 2196995
22	(child* or schoolchild* or school age* or preschool* or kid or kids or toddler*).mp. 2836224
23	Adolescent/ 2239644
24	(adoles* or teen* or boy* or girl*).mp. 2508862
25	Minors/ 2845
26	Puberty/ 14494
27	(minor* or pubert* or pubescen*).mp. 438403
28	exp Pediatrics/ 63268
29	(pediatric* or paediatric*).mp. 540413
30	exp Schools/ 150012
31	(nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*).mp. 90943
32	or/19-31 5496221

Searches		
33	randomized controlled trial.pt.	610144
34	controlled clinical trial.pt.	95515
35	randomized.ab.	640466
36	placebo.ab.	247067
37	drug therapy.fs.	2680945
38	randomly.ab.	430422
39	trial.ti.	306146
40	groups.ab.	2658649
41	or/33-40	5771700
42	(animals not (humans and animals)).sh.	5174637
43	41 not 42	5044745
44	10 and 18 and 32 and 43	1715
45	limit 44 to ed=20220420-20240430	112
46	limit 44 to dt=20220420-20240430	115
47	45 or 46	125
Note: in the re-run the following lines were used:		
44	10 and 18 and 32 and 43	
45	limit 44 to ed=20240401-20241017	
46	limit 44 to dt=20240401-20241017	
47	45 or 46	

Additional search techniques

Forward citation searching

Date of search	4/4/24 and re-run 17/10/24
How the seed papers were identified	Gao et al. (2023) was identified in the Systematic Review (Part 1) search
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	Main search: Data updated 2024-04-01 Update search: 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. A new forward citation search was done with Gao et al. at the time of re-running the database searches.
How the results were selected	All citations were downloaded.
List of seed papers used	Gao Y et al. (2023) Shorter Versus Longer-term Antibiotic Treatments for Community-Acquired

	Pneumonia in Children: A Meta-analysis. *Pediatrics*, 151(6), e2022060097
No. of forward citation searching results	Main search: 1 Re-run: 3 Total: 4

Reference list checking

Date of search	4/4/24
How the seed papers were identified	Gao et al. (2023) was identified in the Systematic Review (Part 1) search
How results were managed	The purpose of this was to add the 16 studies included in Gao et al. (2023) to the EPPI-R file. The papers were identified manually from the reference list.
How the results were selected	All 16 citations were added.
List of seed papers used	Gao Y et al. (2023) Shorter Versus Longer-term Antibiotic Treatments for Community-Acquired Pneumonia in Children: A Meta-analysis. *Pediatrics*, 151(6), e2022060097
No. of reference list checking results	16

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 (INAHTA)	20/11/2023	INAHTA	Version available on 20/11/23 with 21319 records	30
MEDLINE ALL	20/11/2023	Ovid	Ovid MEDLINE(R) ALL 1946 to November 17, 2023	1534
NHS Economic Evaluation Database (NHS EED)	20/11/2023	CRD	Archived – last updated 31 March 2015	11

Re-run results

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

Search strategy history

Database name: Econlit

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

Database name: Embase

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

Searches
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 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/

Searches
or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ 3801223
27 european union/ 31487
28 developed country/ 35727
29 or/25-28 3834983
30 24 not 29 1561961
31 23 not 30 6971
32 limit 31 to english language 6647
33 (letter or editorial).pt. 2081948
34 32 not 33 6549
35 Case report/ 2939178
36 34 not 35 6182
37 nonhuman/ not human/ 5325269
38 36 not 37 6027
39 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 5742113
40 38 not 39 4181
41 limit 40 to yr="2014 -Current" 2288
Note: in the re-run Line 41 was changed to limit 40 to dc=20231101-20241014.

Database name: International HTA Database

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

Database name: MEDLINE ALL

Searches
1 pneumonia/ or bronchopneumonia/ or pleuropneumonia/ or pneumonia, bacterial/ or chlamydial pneumonia/ or pneumonia, mycoplasma/ or pneumonia, pneumococcal/ or pneumonia, rickettsial/ or pneumonia, staphylococcal/ or pneumonia, necrotizing/ or pneumonia, viral/ or organizing pneumonia/ or cryptogenic organizing pneumonia/ or healthcare-associated pneumonia/ 125178

Searches
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/ 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

Searches
"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

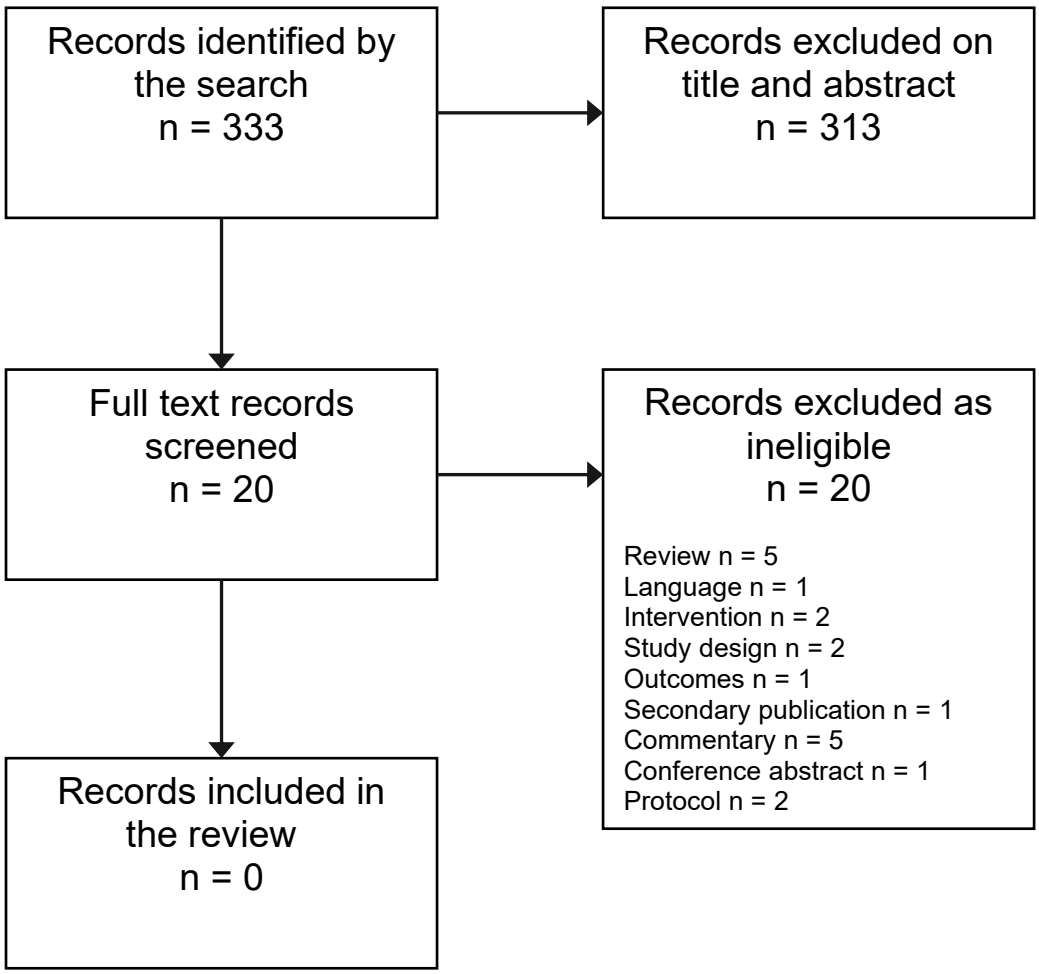
Database name: NHS Economic Evaluation Database (NHS EED)

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
7 MeSH DESCRIPTOR pneumonia, pneumococcal 48
8 MeSH DESCRIPTOR pneumonia, rickettsial 0
9 MeSH DESCRIPTOR pneumonia, staphylococcal 10

Searches
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 studies published since Gao (2023) that would be eligible for inclusion



Appendix D – Effectiveness evidence

Gao, 2023

Bibliographic Reference	Gao, Ya; Liu, Ming; Yang, Kelu; Zhao, Yunli; Tian, Jinhui; Pernica, Jeffrey M; Guyatt, Gordon; Shorter Versus Longer-term Antibiotic Treatments for Community-Acquired Pneumonia in Children: A Meta-analysis.; Pediatrics; 2023; vol. 151 (no. 6)

1.2 Study Characteristics

Study design	Systematic review
Study details	**Dates searched** • up to April 30, 2022 **Databases searched** Medline, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) **Sources of funding** • No external funding
Inclusion criteria	• RCT or cluster RCT • Under 18s • diagnosed CAP • investigator-defined definitions, including but not limited to the WHO acute respiratory infection guidelines, chest examination by a physician, or diagnosis based on radiologic evidence, clinical signs, or symptoms • minimum 2 days difference between short and long durations • Shorter duration = 5 days or less
Exclusion criteria	• HAP • bronchitis • >20% of patients ineligible
Intervention(s)	• Shorter duration antibiotic treatment: 5 days or less • Longer duration antibiotic treatment: more than 5 days
Outcome(s)	• Clinical cure

	• Treatment failure • Relapse • Mortality • Need for hospitalisation • Need for change in antibiotics • All adverse events • Serious adverse events
Number of studies included in the systematic review	16
Studies from the systematic review that are relevant for use in the current review	• Agarwal 2004 • Awasthi 2008 • Bielicki 2021 • Ginsburg 2020 • Gomez Campdera 1996 • Kogan 2003 • MASCOT 2002 • Pernica 2021 • Ronchetti 1994 • Roord 1996 • Sadruddin 2019
Studies from the systematic review that are not relevant for use in the current review	• Greenberg 2014 • Harris 1998 • Kartasasmita 2003 • Williams 2022 • Wubbel 1999
Additional comments	Treatment failure, relapse and need for change in antibiotics outcomes not extracted.

1.2.1 Critical appraisal - GDT Crit App - ROBIS checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	Low
Overall study ratings	Applicability as a source of data	Partially applicable

Appendix E – Forest plots

1.2.2 Primary analyses

Figure 2: Clinical cure: Number of patients who were considered clinically cured within 1 month follow-up

Grouped by 3 days vs 5 days, 3 days vs 10 days, and 3 days vs 7 days. Lower scores favour longer duration antibiotics.

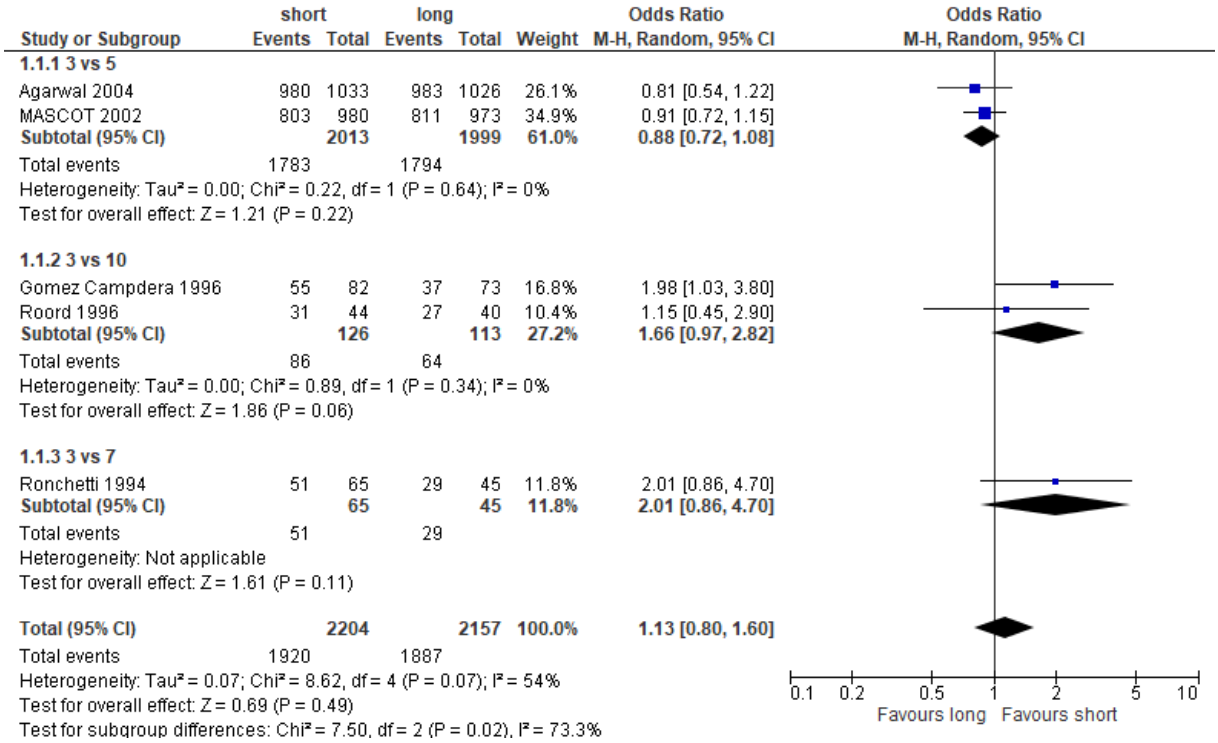


Figure 3: Mortality: Number of patients who had died within 1 month follow-up

Grouped by 3 days vs 5 days, and 3 days vs 7 days. Lower scores favour longer duration antibiotics.

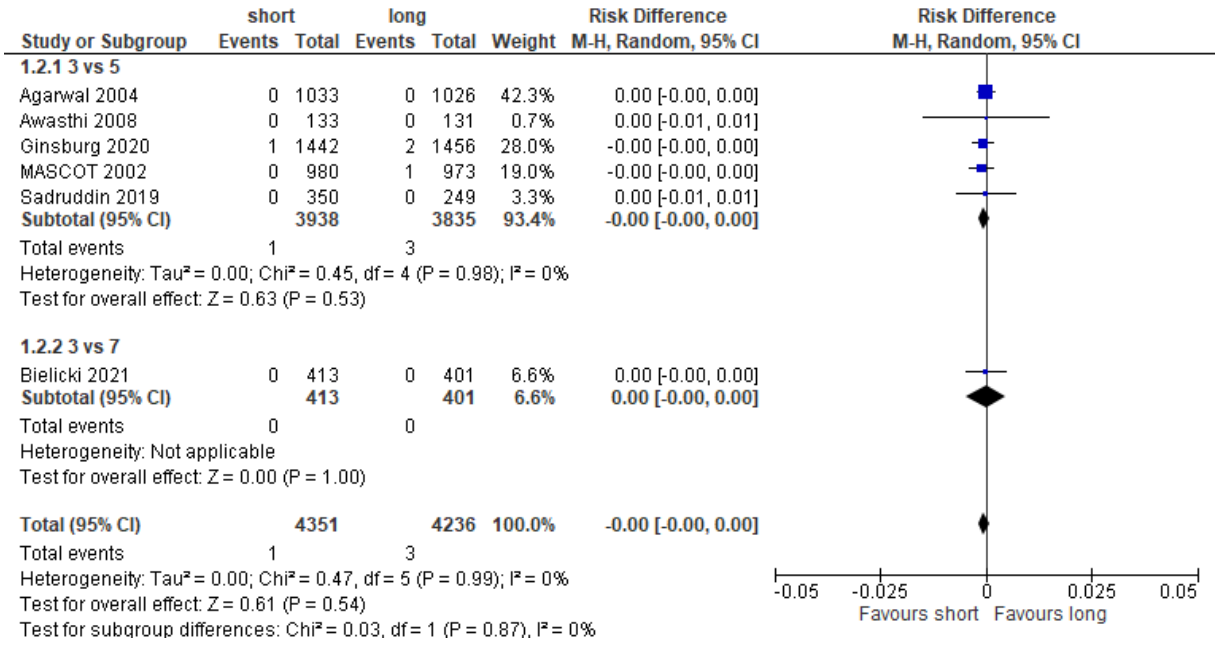


Figure 4: Need for hospitalisation: Number of patients who were admitted to hospital within 1 month follow-up

Grouped by 3 days vs 5 days, and 3 days vs 10 days. Lower scores favour longer duration antibiotics.

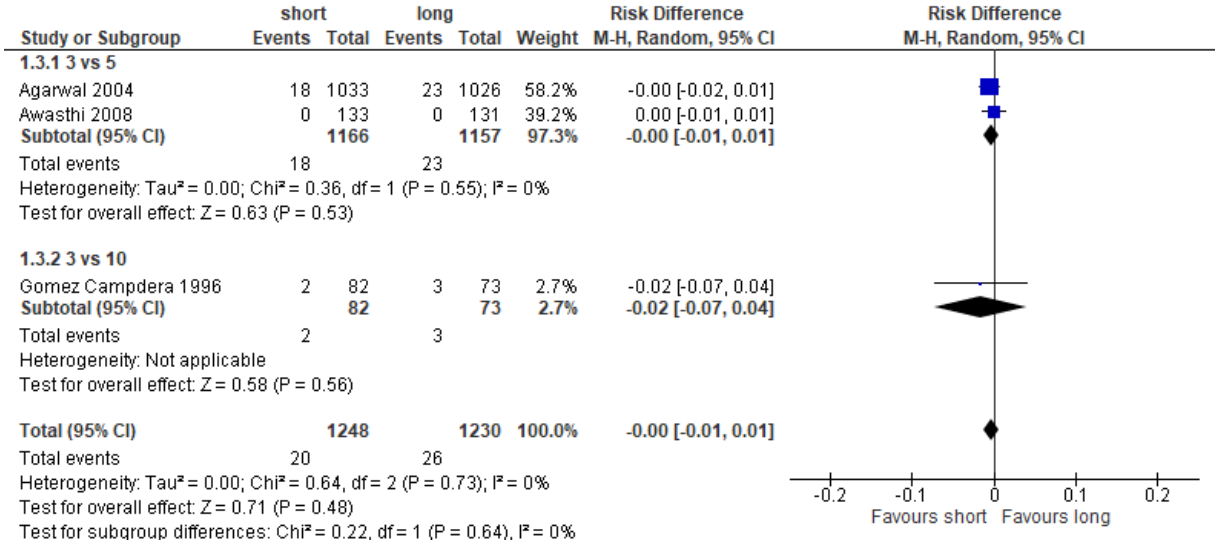


Figure 5: Serious adverse events: Number of patients who had a serious adverse event within 1 month follow-up

Grouped by 3 days vs 5 days, and 3 days vs 7 days. Lower scores favour longer duration antibiotics.

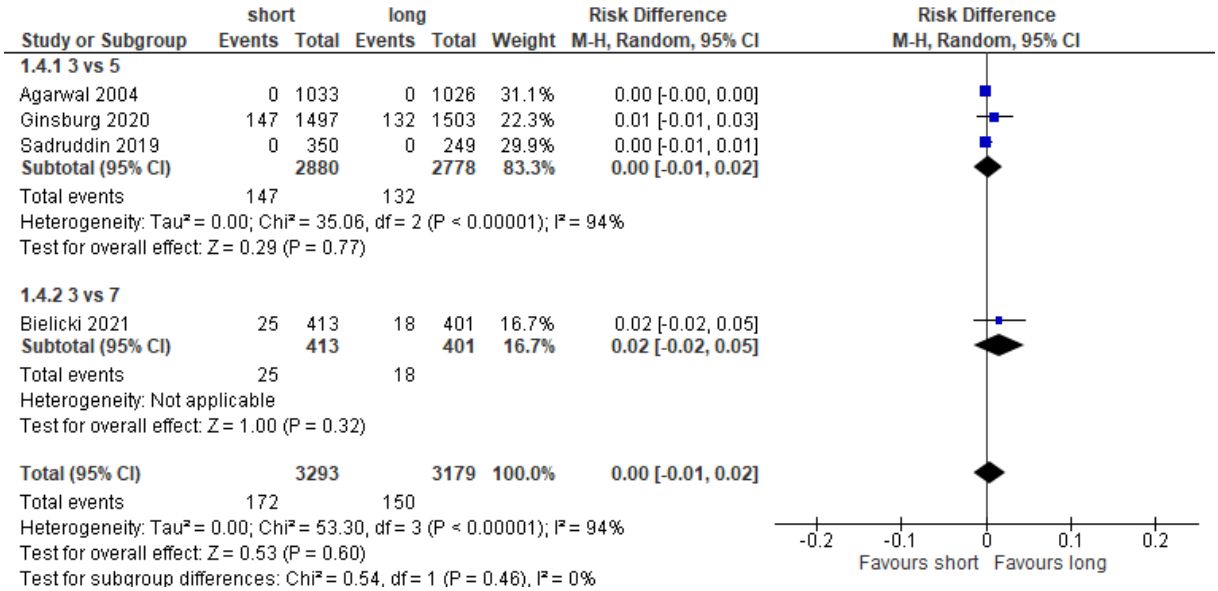
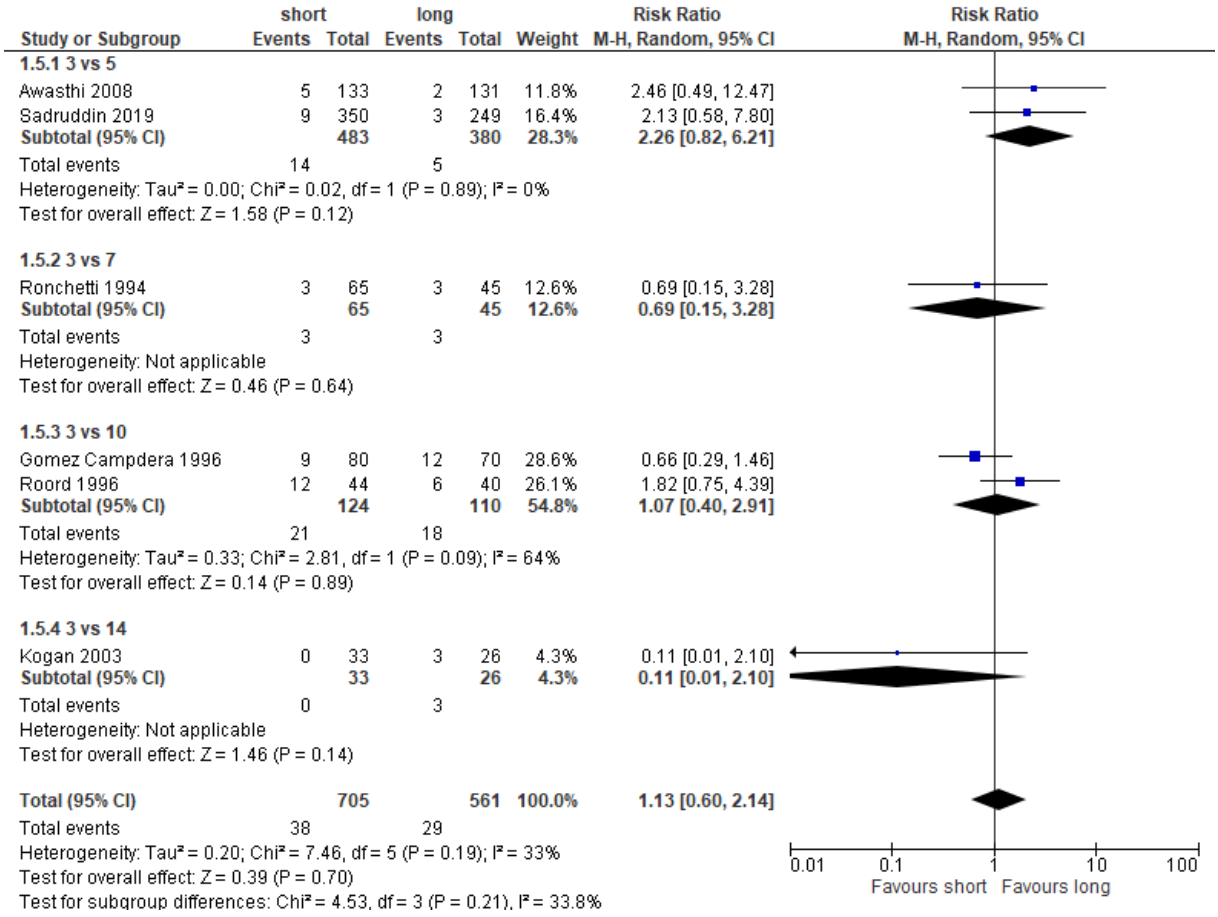


Figure 6: All adverse events: Number of patients who had any adverse event within 1 month follow-up

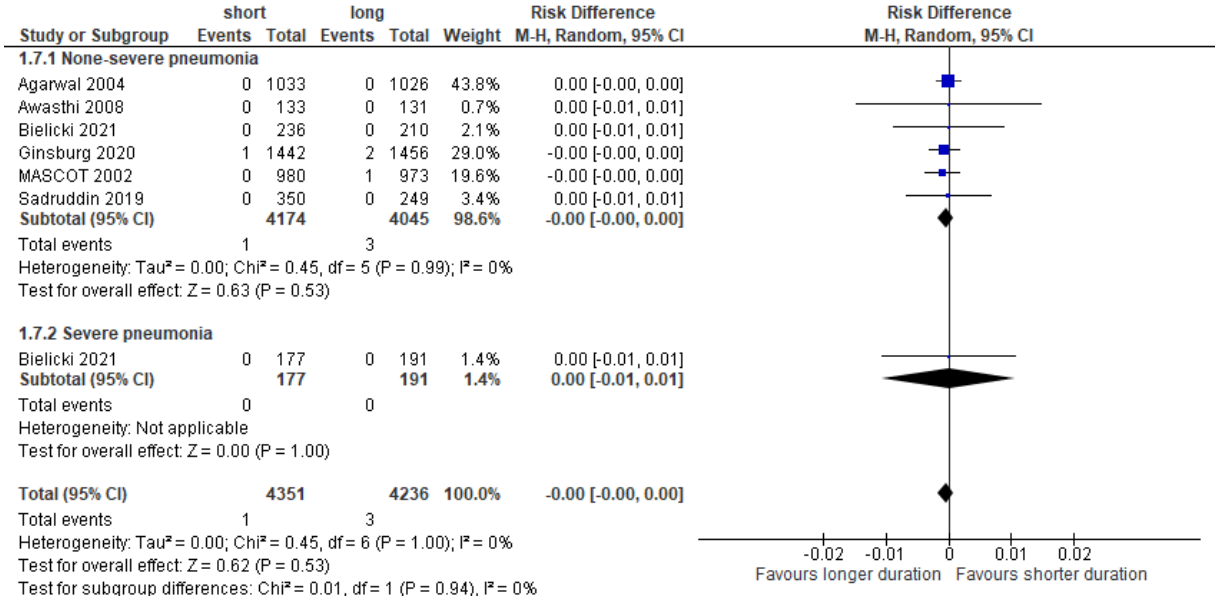
Grouped by 3 days vs 5 days, 3 days vs 7 days, 3 days vs 10 days, and 3 days vs 14 days. Lower scores favour longer duration antibiotics.



1.2.3 Subgroup analyses by severity of CAP

Figure 7: Subgroup analysis of mortality by severity of CAP: Number of patients who had died within 1 month follow-up

Grouped by patients with non-severe pneumonia, and patients with severe pneumonia. Lower scores favour longer duration antibiotics.



1.2.4 Subgroup analyses by age group

Figure 8: Subgroup analysis of clinical cure by age group: Number of patients who were considered clinically cured within 1 month follow-up

Grouped by age < 5 years, and 5 to 18 years. Lower scores favour longer duration antibiotics.

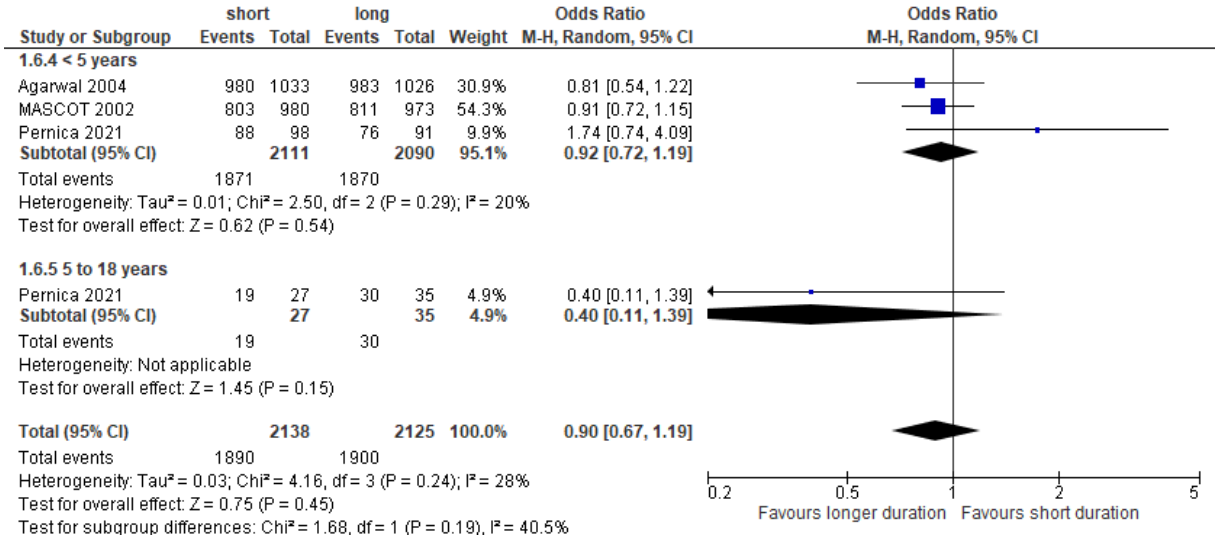
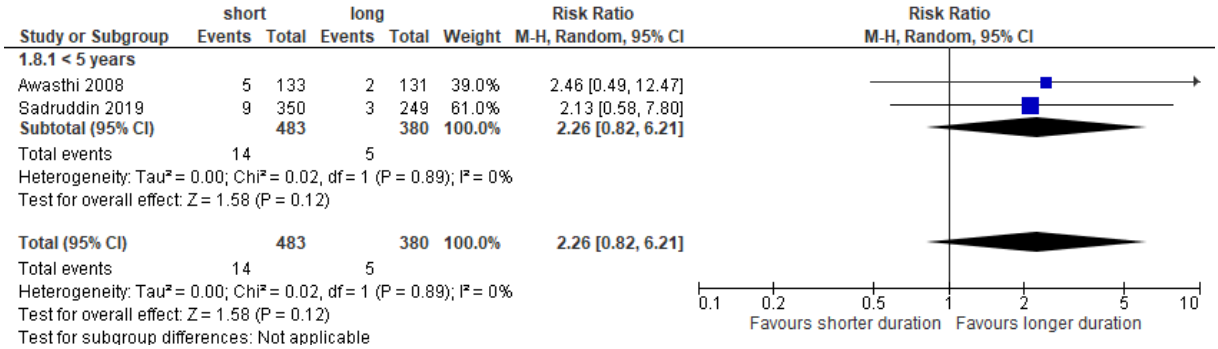


Figure 9: Subgroup analysis of all adverse events by age group: Number of patients who had any adverse event within 1 month follow-up

Grouped by age < 5 years. Lower scores favour longer duration antibiotics



Appendix F – GRADE tables

Certainty assessment						№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Short**	**long**	**Relative (95% CI)**	**Absolute (95% CI)**	
Clinical cure										
5	randomised trials	very serious[a]	serious[b]	not serious	serious[c]	1920/2204 (87.1%)	1887/2157 (87.5%)	**OR 1.13** (0.80 to 1.60)	**13 more per 1,000** (from 27 fewer to 43 more)	⨁◯◯◯ Very low
Clinical cure - 3 vs 5										
2	randomised trials	very serious[a]	not serious	not serious	serious[c]	1783/2013 (88.6%)	1794/1999 (89.7%)	**OR 0.88** (0.72 to 1.08)	**12 fewer per 1,000** (from 34 fewer to 7 more)	⨁◯◯◯ Very low
Clinical cure - 3 vs 10										
2	randomised trials	very serious[a]	not serious	not serious	serious[c]	86/126 (68.3%)	64/113 (56.6%)	**OR 1.66** (0.97 to 2.82)	**118 more per 1,000** (from 7 fewer to 220 more)	⨁◯◯◯ Very low
Clinical cure - 3 vs 7										
1	randomised trials	very serious[a]	not serious	not serious	serious[c]	51/65 (78.5%)	29/45 (64.4%)	**OR 2.01** (0.86 to 4.70)	**140 more per 1,000** (from 35 fewer to 250 more)	⨁◯◯◯ Very low
Mortality										

Certainty assessment						№ of patients		Effect		Certainty	
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Short**	**long**	**Relative (95% CI)**	**Absolute (95% CI)**		
6	randomised trials	not serious	not serious	not serious	not serious	1/4351 (0.0%)	3/4236 (0.1%)	not estimable[g]	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ High	
Mortality - 3 vs 5											
5	randomised trials	not serious	not serious	not serious	not serious	1/3938 (0.0%)	3/3835 (0.1%)	not estimable[g]	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ High	
Mortality - 3 vs 7											
1	randomised trials	not serious	not serious	not serious	not serious	0/413 (0.0%)	0/401 (0.0%)	not estimable[g]	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ High	
Need for hospitalisation											
3	randomised trials	very serious[a]	not serious	not serious	not serious	20/1248 (1.6%)	26/1230 (2.1%)	not estimable[g]	**0 fewer per 1,000** (from 10 fewer to 10 more)	⊕⊕◯◯ Low	
Need for hospitalisation - 3 vs 5											
2	randomised trials	very serious[a]	not serious	not serious	not serious	18/1166 (1.5%)	23/1157 (2.0%)	not estimable[g]	**0 fewer per 1,000** (from 10 fewer to 10 more)	⊕⊕◯◯ Low	

Certainty assessment						№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Short**	**long**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**
Need for hospitalisation - 3 vs 10										
1	randomised trials	very serious[a]	not serious	not serious	not serious	2/82 (2.4%)	3/73 (4.1%)	not estimable[g]	**20 more per 1,000** (from 40 fewer to 70 more)	⨁⨁◯◯ Low
Serious adverse events										
4	randomised trials	very serious[a]	very serious[d]	not serious	not serious	172/3293 (5.2%)	150/3179 (4.7%)	not estimable[g]	**0 fewer per 1,000** (from 20 fewer to 10 more)	⨁◯◯◯ Very low
Serious adverse events - 3 vs 5										
3	randomised trials	very serious[a]	very serious[d]	not serious	not serious	147/2880 (5.1%)	132/2778 (4.8%)	not estimable[g]	**0 fewer per 1,000** (from 20 fewer to 10 more)	⨁◯◯◯ Very low
Serious adverse events - 3 vs 7										
1	randomised trials	not serious	not serious	not serious	not serious	25/413 (6.1%)	18/401 (4.5%)	not estimable[g]	**20 fewer per 1,000** (from 50 fewer to 20 more)	⨁⨁⨁⨁ High
All adverse events										

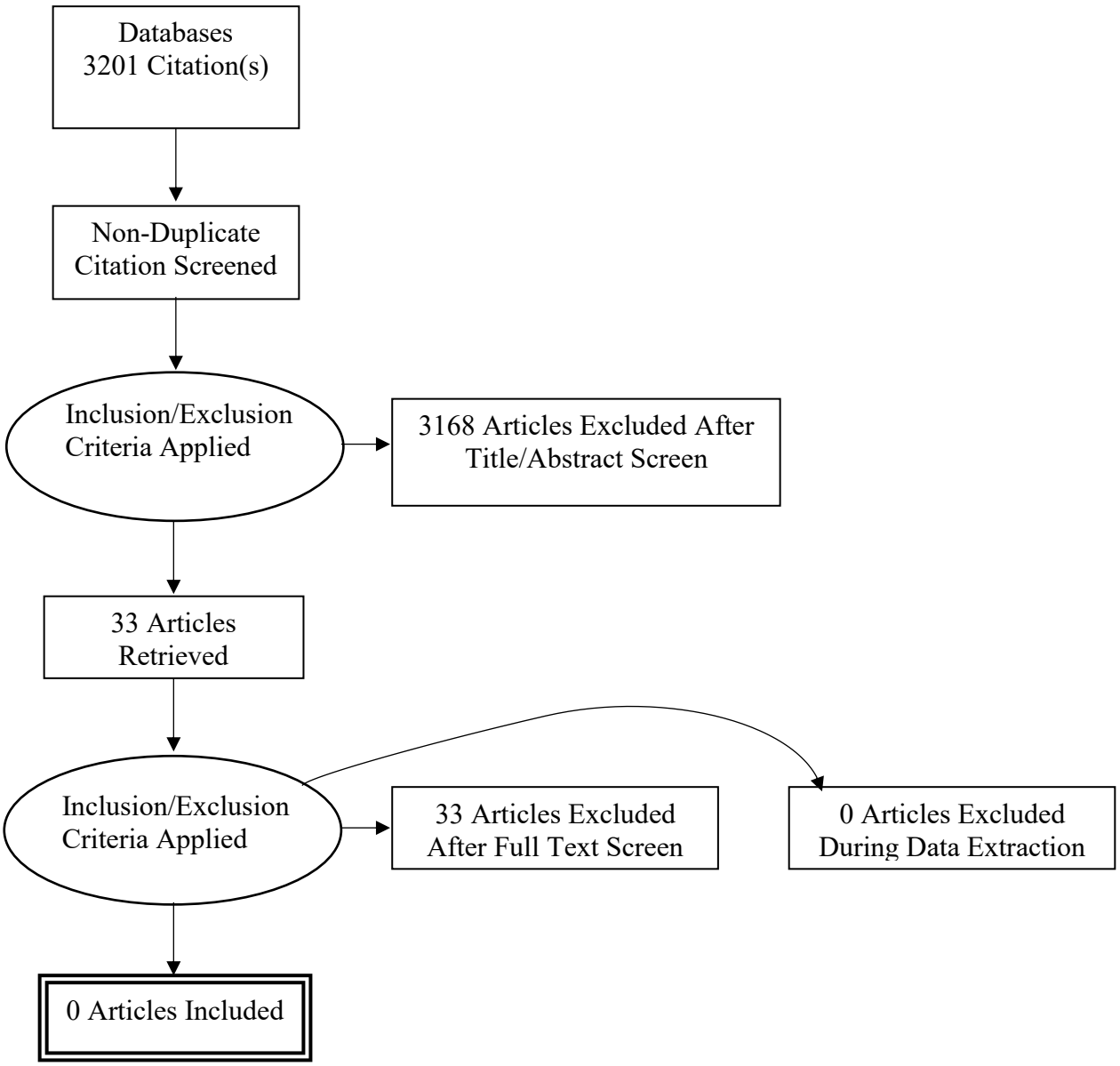
Certainty assessment						№ of patients		Effect		Certainty	
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Short**	**long**	**Relative (95% CI)**	**Absolute (95% CI)**		
6	randomised trials	very serious[a]	not serious	not serious	very serious[e]	38/705 (5.4%)	29/561 (5.2%)	**RR 1.13** (0.60 to 2.14)	**7 more per 1,000** (from 21 fewer to 59 more)	⨁◯◯◯ Very low	
All adverse events - 3 vs 5											
2	randomised trials	very serious[a]	not serious	not serious	serious[c]	14/483 (2.9%)	5/380 (1.3%)	**RR 2.26** (0.82 to 6.21)	**17 more per 1,000** (from 2 fewer to 69 more)	⨁◯◯◯ Very low	
All adverse events - 3 vs 7											
1	randomised trials	very serious[a]	not serious	not serious	very serious[e]	3/65 (4.6%)	3/45 (6.7%)	**RR 0.69** (0.15 to 3.28)	**21 fewer per 1,000** (from 57 fewer to 152 more)	⨁◯◯◯ Very low	
All adverse events - 3 vs 10											
2	randomised trials	very serious[a]	serious[f]	not serious	very serious[e]	21/124 (16.9%)	18/110 (16.4%)	**RR 1.07** (0.40 to 2.91)	**11 more per 1,000** (from 98 fewer to 313 more)	⨁◯◯◯ Very low	
All adverse events - 3 vs 14											
1	randomised trials	very serious[a]	not serious	not serious	very serious[e]	0/33 (0.0%)	3/26 (11.5%)	**RR 0.11** (0.01 to 2.10)	**103 fewer per 1,000** (from 114 fewer to 127 more)	⨁◯◯◯ Very low	

Certainty assessment						№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Short**	**long**	**Relative (95% CI)**	**Absolute (95% CI)**	
All adverse events subgroup analysis by age group										
2	randomised trials	very serious[a]	not serious	not serious	serious[c]	14/483 (2.9%)	5/380 (1.3%)	**RR 2.26** (0.82 to 6.21)	**17 more per 1,000** (from 2 fewer to 69 more)	⨁◯◯◯ Very low
All adverse events subgroup analysis by age group - < 5 years										
2	randomised trials	very serious[a]	not serious	not serious	serious[c]	14/483 (2.9%)	5/380 (1.3%)	**RR 2.26** (0.82 to 6.21)	**17 more per 1,000** (from 2 fewer to 69 more)	⨁◯◯◯ Very low
Clinical Cure subgroup analysis by age group										
3	randomised trials	very serious[a]	not serious	not serious	serious[c]	1890/2138 (88.4%)	1900/2125 (89.4%)	**OR 0.90** (0.67 to 1.19)	**10 fewer per 1,000** (from 44 fewer to 15 more)	⨁◯◯◯ Very low
Clinical Cure subgroup analysis by age group - < 5 years										
3	randomised trials	very serious[a]	not serious	not serious	serious[c]	1871/2111 (88.6%)	1870/2090 (89.5%)	**OR 0.92** (0.72 to 1.19)	**8 fewer per 1,000** (from 35 fewer to 15 more)	⨁◯◯◯ Very low
Clinical Cure subgroup analysis by age group - 5 to 18 years										

Certainty assessment						№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Short**	**long**	**Relative (95% CI)**	**Absolute (95% CI)**	
1	randomised trials	not serious	not serious	not serious	very serious[e]	19/27 (70.4%)	30/35 (85.7%)	**OR 0.40** (0.11 to 1.39)	**151 fewer per 1,000** (from 460 fewer to 36 more)	⊕⊕◯◯ Low
Mortality subgroup analysis by severity of CAP										
7	randomised trials	not serious	not serious	not serious	not serious	1/4351 (0.0%)	3/4236 (0.1%)	not estimable[g]	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ High
Mortality subgroup analysis by severity of CAP - None-severe pneumonia										
6	randomised trials	not serious	not serious	not serious	not serious	1/4174 (0.0%)	3/4045 (0.1%)	not estimable[g]	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ High
Mortality subgroup analysis by severity of CAP - Severe pneumonia										
1	randomised trials	not serious	not serious	not serious	not serious	0/177 (0.0%)	0/191 (0.0%)	not estimable[g]	**0 fewer per 1,000** (from 10 fewer to 10 more)	⊕⊕⊕⊕ High

CI: confidence interval; OR: odds ratio; RR: risk ratio
a. Downgraded twice for risk of bias due to inadequate allocation concealment and lack of blinding
b. Downgraded once as I2 was between 33.3% and 66.7% (I2 = 54%)
c. 95% CI crosses 1 MID (0.8 or 1.25)
d. Downgraded twice as I2 was over 66.8% (I2 = 94%)
e. 95% CI crosses 2 MIDs (0.8 and 1.25)
f. Downgraded once as I2 was between 33.3% and 66.7% (I2 = 64%)
g. Not estimable due to low event rates

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

Study	Code [Reason]
Ahmed, Sheraz, Ariff, Shabina, Muhammed, Sajid et al. (2022) Community case management of fast-breathing pneumonia with 3 days oral amoxicillin vs 5 days cotrimoxazole in children 2-59 months of age in rural Pakistan: A cluster randomized trial. Journal of global health 12: 04097	- No relevant outcomes reported *Only treatment failure outcomes which do not match the protocol*
Barry, Henry C (2022) Comparable Outcomes With Five and 10 Days of Antibiotics in Children With CAP. American family physician 106(3): online	- Commentary
Blanc, A.; Cameron, J.; Yeats, A. (2022) A narrative review of short versus long-course antibiotic treatment for community-acquired pneumonia in the outpatient pediatric setting. Journal de Pharmacie Clinique 41(2): 57-65	- Study not reported in English *French*
Daley, M.F., Reifler, L.M., Sterrett, A.T. et al. (2024) Improving Antibiotic Prescribing for Children with Community-acquired Pneumonia in Outpatient Settings. The Journal of pediatrics: 114155	- Not a relevant study design *A quasi-experimental, interrupted time series design*
Joerger, Torsten and Swami, Sanjeev K (2022) Evaluation of a 5-day High-Dose Course of Amoxicillin for the Management of Community-Acquired Pneumonia in Children of 6 months to 10 years of Age. Journal of the Pediatric Infectious Diseases Society 11(11): 480-481	- Commentary
Kok, Hing C, McCallum, Gabrielle B, Yerkovich, Stephanie T et al. (2024) Twenty-four Month Outcomes of Extended- Versus Standard-course Antibiotic Therapy in Children Hospitalized With Pneumonia in High-risk Settings: A Randomized Controlled Trial. The Pediatric infectious disease journal 43(9): 872-879	- Study does not contain a relevant intervention *Short duration = 5-6 days, does not match protocol*
Kuijpers, S.M.E., Buis, D.T.P., Ziesemer, K.A. et al. (2024) The evidence base for the optimal antibiotic treatment duration of upper and lower respiratory tract infections: an umbrella review. The Lancet Infectious Diseases	- Not a relevant study design *Review of reviews*
Kuitunen, Ilari, Jaaskelainen, Johanna, Korppi, Matti et al. (2023) Antibiotic Treatment Duration for Community-Acquired Pneumonia in Outpatient Children in High-Income Countries-A Systematic Review and Meta-Analysis. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 76(3): e1123-e1128	- Systematic review used as source of primary studies
Kuitunen, Ilari and Renko, Marjo (2024) How Long Antibiotic Treatment Is Needed for Community-acquired Pneumonia in Children?. The Pediatric infectious disease journal 43(1): e14-e15	- Systematic review used as source of primary studies

Study	Code [Reason]
Li, Qinyuan, Zhou, Qi, Florez, Ivan D et al. (2022) Short-Course vs Long-Course Antibiotic Therapy for Children With Nonsevere Community-Acquired Pneumonia: A Systematic Review and Meta-analysis. JAMA pediatrics 176(12): 1199-1207	- Systematic review used as source of primary studies
Lyon, Edward and Olarte, Liset (2024) Community-acquired bacterial pneumonia in children: an update on antibiotic duration and immunization strategies. Current opinion in pediatrics 36(2): 144-149	- Only the abstract is available
McCallum, Gabrielle B, Fong, Siew M, Grimwood, Keith et al. (2022) Extended Versus Standard Antibiotic Course Duration in Children <5 Years of Age Hospitalized With Community-acquired Pneumonia in High-risk Settings: Four-week Outcomes of a Multicenter, Double-blind, Parallel, Superiority Randomized Controlled Trial. The Pediatric infectious disease journal 41(7): 549-555	- Study does not contain a relevant intervention *Short course is defined as 5-6 days*
NCT06291012 (2024) Stopping Pneumonia Antibiotherapy Regimen Early. https://clinicaltrials.gov/ct2/show/NCT06291012	- Full text paper not available *Trial protocol*
NCT06494072 (2024) Short Versus Standard of Care Antibiotic Duration for Children Hospitalized for CAP. https://clinicaltrials.gov/ct2/show/NCT06494072	- Full text paper not available *Trial protocol*
Pettigrew, M M, Kwon, J, Gent, J F et al. (2022) Comparison of the Respiratory Resistomes and Microbiota in Children Receiving Short versus Standard Course Treatment for Community-Acquired Pneumonia. mBio 13(2): e0019522	- Secondary publication of an included study that does not provide any additional relevant information
Poutanen, Roope, Korppi, Matti, Csonka, Peter et al. (2023) Use of antibiotics contrary to guidelines for children's lower respiratory tract infections in different health care settings. European journal of pediatrics 182(10): 4369-4377	- Not a relevant study design *Retrospective data*
R Marques, Isabela, P Calvi, Izabela, A Cruz, Sara et al. (2022) Shorter versus longer duration of Amoxicillin-based treatment for pediatric patients with community-acquired pneumonia: a systematic review and meta-analysis. European journal of pediatrics 181(11): 3795-3804	- Systematic review used as source of primary studies
Rosenberg, Karen (2023) Consider Short Course of Antibiotics for Children with Nonsevere Community-Acquired Pneumonia. The American journal of nursing 123(3): 62	- Commentary
Schwarz, E.P. (2023) Update: amoxicillin for children with pneumonia Is a short course as effective as a long one?. Geneesmiddelenbulletin 57(7): e2023	- Commentary

Study	Code [Reason]
Wilkins, Hannah; Hobart-Porter, Nicholas; Eastin, Carly (2024) What is the Optimal Treatment Duration for Outpatient Pediatric Community-Acquired Pneumonia?. Annals of emergency medicine 83(3): 214-216	- Commentary

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	- Study does not contain a relevant intervention

Study	Code [Reason]
children under 5 years of age. Human vaccines & immunotherapeutics 14(1): 106-110	*Non-comparative costing analysis*
Cisco, Giulio, Meier, Armando N, Senn, Nicolas et al. (2024) Cost-effectiveness analysis of procalcitonin and lung ultrasonography guided antibiotic prescriptions in primary care. The European journal of health economics : HEPAC : health economics in prevention and care	- setting in primary care whereas the review was in secondary care
Costa, Nadege, Hoogendijk, Emiel O, Mounie, Michael et al. (2017) Additional Cost Because of Pneumonia in Nursing Home Residents: Results From the Incidence of Pneumonia and Related Consequences in Nursing Home Resident Study. Journal of the American Medical Directors Association 18(5): 453e7-453e12	- Study does not contain a relevant intervention *Non-comparative costing analysis*
Hyams, Catherine; Williams, O Martin; Williams, Philip (2020) Urinary antigen testing for pneumococcal pneumonia: is there evidence to make its use uncommon in clinical practice?. ERJ open research 6(1)	- Review article but not a systematic review, all primary studies were check for relevance
Ito, Akihiro, Ishida, Tadashi, Tokumasu, Hironobu et al. (2017) Impact of procalcitonin-guided therapy for hospitalized community-acquired pneumonia on reducing antibiotic consumption and costs in Japan. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy 23(3): 142-147	- Not a relevant study design *Costing study not a cost utility study*
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	- Study not reported in English *Reported in Spanish*

Study	Code [Reason]
traditional hospitalization: An exploratory study of 40 cases. Value in Health Regional Issues 8: 112-115	
McKinnell, James A, Corman, Shelby, Patel, Dipen et al. (2018) Effective Antimicrobial Stewardship Strategies for Cost-effective Utilization of Telavancin for the Treatment of Patients With Hospital-acquired Bacterial Pneumonia Caused by Staphylococcus aureus. Clinical therapeutics 40(3): 406-414e2	- Study does not contain a relevant intervention *US study that compares different antibiotics rather than length of treatments*
Meacock, Rachel, Sutton, Matt, Kristensen, Soren Rud et al. (2017) Using Survival Analysis to Improve Estimates of Life Year Gains in Policy Evaluations. Medical decision making : an international journal of the Society for Medical Decision Making 37(4): 415-426	- Study does not contain a relevant intervention *Modelling survival not cost effectiveness of treatment*
Miners, Lisa, Huntington, Susie, Lee, Nathaniel et al. (2023) An economic evaluation of two PCR-based respiratory panel assays for patients admitted to hospital with community-acquired pneumonia (CAP) in the UK, France and Spain. BMC pulmonary medicine 23(1): 220	- Not a relevant study design *Cost consequence study*
Patel, Archana B, Bang, Akash, Singh, Meenu et al. (2015) A randomized controlled trial of hospital versus home based therapy with oral amoxicillin for severe pneumonia in children aged 3 - 59 months: The IndiaCLEN Severe Pneumonia Oral Therapy (ISPOT) Study. BMC pediatrics 15: 186	- Non OECD country *India*
Pliakos, Elina Eleftheria, Andreatos, Nikolaos, Tansarli, Giannoula S et al. (2019) The Cost-Effectiveness of Corticosteroids for the Treatment of Community-Acquired Pneumonia. Chest 155(4): 787-794	- US study
Prasath, T.M., Ramachandran, V., Geetha, S. et al. (2019) Hidden Markov model-based cough sound analysis for classification of asthma and pneumonia in pediatric. Drug Invention Today 11(7): 1692-1695	- Full text paper not available
Przybilla, Jens, Ahnert, Peter, Bogatsch, Holger et al. (2020) Markov State Modelling of Disease Courses and Mortality Risks of Patients with Community-Acquired Pneumonia. Journal of clinical medicine 9(2)	- Study does not contain a relevant intervention *Does not include costs*
Reynolds, Courtney A, Finkelstein, Jonathan A, Ray, G Thomas et al. (2014) Attributable healthcare utilization and cost of pneumonia due to drug-resistant streptococcus pneumonia: a cost analysis. Antimicrobial resistance and infection control 3: 16	- Study does not contain a relevant intervention *Looking at different antibiotics not the length of the courses*
Rozenbaum, Mark H, Mangen, Marie-Josee J, Huijts, Susanne M et al. (2015) Incidence, direct costs and duration of hospitalization of patients hospitalized with community acquired pneumonia: A nationwide retrospective claims database analysis. Vaccine 33(28): 3193-9	- Study does not contain a relevant intervention *Costing analysis without comparators*

Study	Code [Reason]
Shi, Honghao, Guo, Wanjie, Zhu, He et al. (2019) Cost-Effectiveness Analysis of Xiyanping Injection (Andrographolide Sulfonate) for Treatment of Adult Community Acquired Pneumonia: A Retrospective, Propensity Score-Matched Cohort Study. Evidence-based complementary and alternative medicine : eCAM 2019: 4510591	- Study does not contain a relevant intervention *Andrographolide Sulfonate injection*
Shiri, Tinevimbo, Khan, Kamran, Keaney, Katherine et al. (2019) Pneumococcal Disease: A Systematic Review of Health Utilities, Resource Use, Costs, and Economic Evaluations of Interventions. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research 22(11): 1329-1344	- Study does not contain a relevant intervention *Vaccines and antibiotics (not length of treatment)*
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*