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Clinical Critically Appraised Topics   Critically Appraised Topics

12-2023

Community Acquired Pneumonia Antibiotic Duration

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Specific Care Question

In pediatric patients with uncomplicated community acquired pneumonia (CAP), is three days of antibiotic treatment noninferior to a longer duration for clinical cure?

Rationale for Question Asked

Since the publication of the most recent guidelines for pediatric CAP by the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA) (Bradley et al., 2011), additional literature addressing the length of antibiotic therapy for CAP has been published. The new evidence has suggested that shorter treatment courses (3 – 5 days) may be sufficient compared to longer treatment courses (7 – 10 days).

Recommendations from the Community Acquired Pneumonia Clinical Pathway Committee:

For patients with uncomplicated, mild, or moderate CAP, a strong recommendation is made for a shorter course of antibiotic treatment (3 - 5 days) for patients $\leq$ 5 years of age. Considerations for longer antibiotic treatment (5 – 7 days) should be made for hospitalized patients with CAP or patients $\geq$ 5 years of age. Data on shorter courses for hospitalized children or children > 5 years of age re not as robust. Generally, 5 days is sufficient in most cases of uncomplicated CAP.

Overview and Certainty of Evidence

The systematic review by Li et al. (2022) included eight randomized control trials (RCTs) that compared short-course antibiotic treatment to long-course antibiotic treatment and reported the outcome of treatment failure (N = 10,662), defined by continuation of pneumonia or new signs of complication, persistent fever after treatment completion, necessitation of change to antibiotics, hospital admission, missed treatment doses, loss to follow-up, or death. Four of the included studies compared treatment of 3 days (n = 4,545) to treatment of 5 days (n = 4,563). Three of the included studies compared treatment of 5 days (n = 357) to treatment of 10 days (n = 366). A single study compared treatment of 3 days (n = 413) to treatment of 7 days (n = 401). A single study compared treatment of 3 days (n = 10) to treatment of 10 days (n = 7).

For the outcome of treatment failure, the systematic review did not find a difference when comparing patients receiving short course treatment and patients receiving long course treatment, RR =1.01, 95% CI [0.92, 1.12], p = .84. When comparing subgroups, no difference was observed when comparing a 3-day course to a 5-day course (RR = 1.01, 95% CI [0.91, 1.12], p = .81), and no difference was observed when comparing a 5-day course to a 10-day course (RR = 0.87, 95% CI [0.50, 1.53], p = .64).

Certainty of the Evidence for Antibiotic Duration. The systematic review authors assessed the certainty of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Guyatt et al., 2008). The systematic review authors found the certainty of evidence to be high for the outcome of treatment failure for all patients combined and for the subgroup of patients aged 2 - 59 months. However, for the subgroup of patients aged 5 - 10 years the certainty of the evidence was low due to very serious imprecision attributed to the wide confidence interval of the result and small sample size of results.

Study characteristics. The search for suitable studies was completed on October 9th, 2023. T. Glenski, MD, performed an initial review on the 349 titles and/or abstracts and identified 32 single studies or systematic reviews believed to answer the question. J. Markham, MD, and F. Turcotte, MD, further reviewed the 32 titles and/or abstracts found in the search and identified two single studies and two systematic reviews believed to answer the question. After an in-depth review of the single studies and systematic reviews, one systematic review answered the question(s).

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Critically Appraised Topic (CAT):
Community Acquired Pneumonia Antibiotic Duration

Included Studies

Author (Year)	Study Type	Population	N	Intervention	Control	Outcomes of Interest	Results
Li et al. (2022)	Systematic Review/Meta-Analysis	Patients aged 2 months – 10 years with non-severe CAP	$N = 10,662$	Short course antibiotic treatment (3 or 5 days)	Long course antibiotic treatment (5, 7 or 10 days)	Treatment failure	• Eight RCTs reported treatment failure. Treatment failure occurred in 12.8% of patients receiving short course treatment and in 12.6% of patients receiving long course treatment ($RR = 1.01$, 95% CI [0.92, 1.12], $p = .84$). • A 3-day course was noninferior to a 5-day course ($RR = 1.01$, 95% CI [0.91, 1.12], $p = .81$). • A 5-day course was noninferior to a 10-day course ($RR = 0.87$, 95% CI [0.50, 1.53], $p = .64$).

Table 1. Treatment failure

Treatment failure: 8 studies, $N = 10,662$

Control	Experiment	Result
Long course (5, 7 or 10 days) n = 5,337	Short course (3 or 5 days) n = 5,323	RR = 1.01, 95% CI [0.92, 1.12], $p = 0.84$
Subgroup analysis: 3 days vs. 5 days 4 studies, $N = 9108$		
5 days $n = 4563$	3 days $n = 4545$	RR 1.01, 95% CI [0.91, 1.12], $p = 0.81$
Subgroup analysis: 5 days vs. 10 days 3 studies, $N = 723$		
10 days $n = 366$	5 days $n = 357$	RR 0.87, 95% CI [0.50, 1.53], $p = 0.64$

Identification of Studies

Search Strategy and Results (see Figure 1)

No.	Query Results
#12	#10 AND ('clinical trial'/de OR 'clinical trial topic'/de OR 'comparative effectiveness'/de OR 'comparative study'/de OR 'consensus development'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'cross sectional study'/de OR 'double blind procedure'/de OR 'evidence based practice'/de OR 'intention to treat analysis'/de OR 'intervention study'/de OR 'major clinical study'/de OR 'meta analysis'/de OR 'multicenter study'/de OR 'multicenter study topic'/de OR 'observational study'/de OR 'practice guideline'/de OR 'prospective study'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial topic'/de OR 'systematic review'/de) AND ('article'/it OR 'article in press'/it OR 'erratum'/it OR 'preprint'/it OR 'review'/it) 349
#11	#10 AND ('clinical trial'/de OR 'clinical trial topic'/de OR 'comparative effectiveness'/de OR 'comparative study'/de OR 'consensus development'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'cross sectional study'/de OR 'double blind procedure'/de OR 'evidence based practice'/de OR 'intention to treat analysis'/de OR 'intervention study'/de OR 'major clinical study'/de OR 'meta analysis'/de OR 'multicenter study'/de OR 'multicenter study topic'/de OR 'observational study'/de OR 'practice guideline'/de OR 'prospective study'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial topic'/de OR 'systematic review'/de) 453
#10	#9 AND ([adolescent]/lim OR [child]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim OR 'child'/exp OR child OR 'children'/exp OR children OR 'pediatrics'/exp OR pediatrics OR 'pediatric' OR pediatric OR 'paediatric' OR paediatric) AND [2017-2023]/py 665
#9	#5 AND #8 6379
#8	#6 AND #7 1318419
#7	'dosage schedule comparison'/exp OR 'drug administration schedule' OR 'short course' OR 'short-course' OR 'long course' OR 'long-course' OR 'time'/exp OR time:ti,ab,kw OR 'time factor'/exp OR 'treatment duration'/exp OR 'duration' OR duration:ti,ab,kw OR course:ti,ab,kw OR '3day*' OR '5 day*' OR '7 day*' OR '10 day*' OR 'drug administration'/exp OR 'short course therapy'/exp OR 'short duration' OR 'long duartion' 8831362
#6	'antibiotic agent'/exp OR 'antibiotic agent':ti,ab,kw OR 'antibiotic therapy'/exp OR 'antibiotic therapy':ti,ab,kw OR 'antibiotic'/exp OR antibiotic:ti,ab,kw OR 'antiinfective agent'/exp OR 'amoxicillin'/exp OR amoxicillin:ti,ab,kw 4961461
#5	#3 OR #4 28964
#4	'community acquired pneumonia'/exp OR 'community acquired pneumonia' 25422
#3	#1 AND #2 28954
#2	'bacterial pneumonia'/exp OR 'bacterial pneumonia':ti,ab,kw OR 'pneumonia'/exp OR pneumonia:ti,ab,kw OR 'virus pneumonia'/exp OR 'viral pneumonia':ti,ab,kw OR 'lower respiratory tract infection'/exp 640279
#1	'community acquired infection'/exp OR 'community acquired':ti,ab,kw

Search Dates: 2018 - Current (*Justification for chosen timeframe:* This question was reviewed by EBP for a CAT in 2018.)

Records identified through database searching *n* = 349

Additional records identified through other sources *n* = 0

Records excluded due to not answering PICOT question or inclusion in systematic review *n* = 345

Studies Not Included in this Review with Exclusion Rationale

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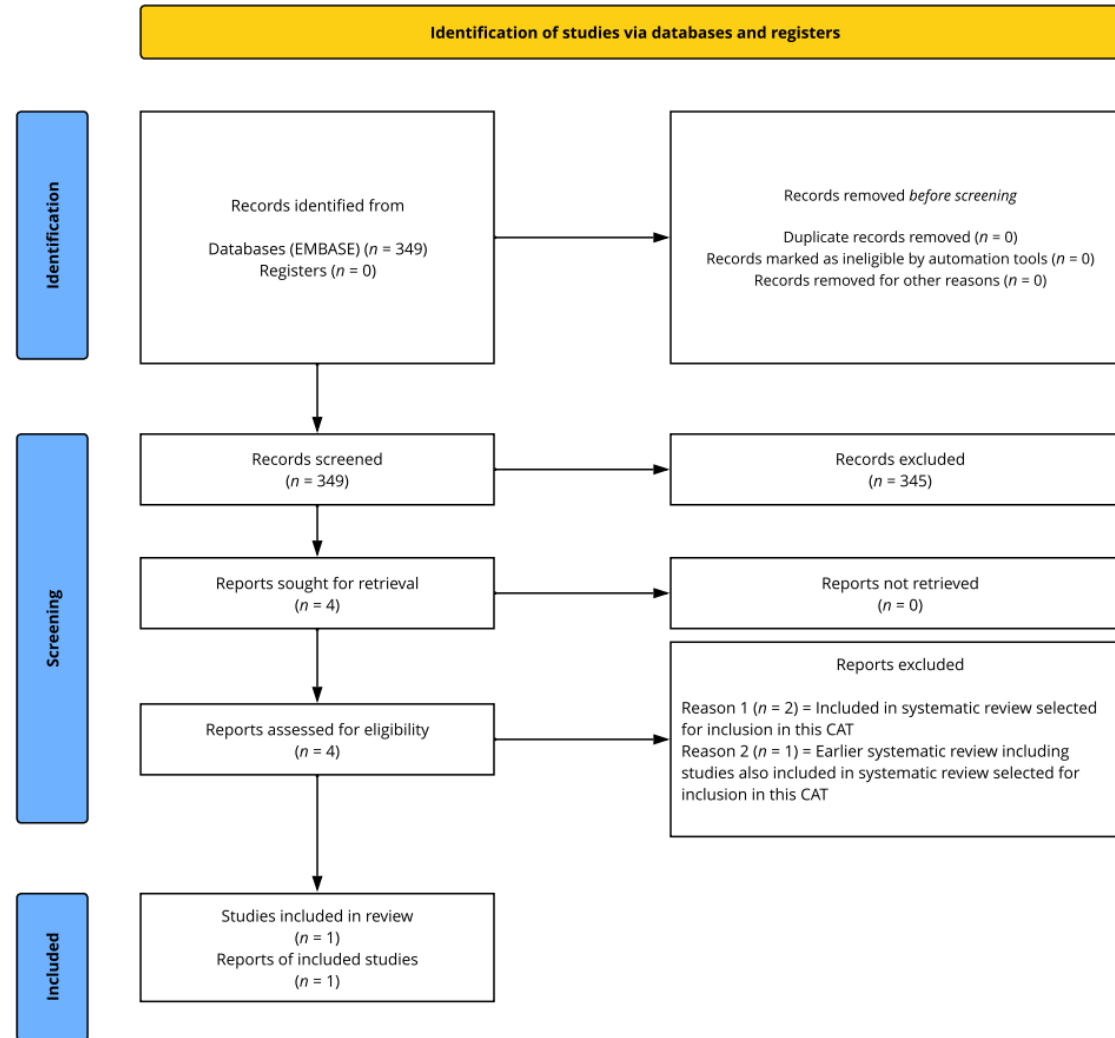| Citation	Reason for exclusion
Barrat et al. (2021)	Report of the study by Bielicki et al. (2021)
Bielicki et al. (2021)	Included in the systematic review from Li et al. (2022).
Kuitunen et al. (2023)	The relevant studies included in this systematic review are also included in the systematic review from Li et al. (2022). The remaining studies in this systematic review do not compare the antibiotic duration in question.

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Figure 1

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA)

Identification of studies via databases and registers

Identification

Records identified from
Databases (EMBASE) (*n* = 349)
Registers (*n* = 0)

Records removed *before screening*
Duplicate records removed (*n* = 0)
Records marked as ineligible by automation tools (*n* = 0)
Records removed for other reasons (*n* = 0)

Screening

Records screened
(*n* = 349)

Records excluded
(*n* = 345)

Reports sought for retrieval
(*n* = 4)

Reports not retrieved
(*n* = 0)

Reports assessed for eligibility
(*n* = 4)

Reports excluded

Reason 1 (*n* = 2) = Included in systematic review selected for inclusion in this CAT
Reason 2 (*n* = 1) = Earlier systematic review including studies also included in systematic review selected for inclusion in this CAT

Included

Studies included in review
(*n* = 1)
Reports of included studies
(*n* = 1)

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Question Originator
  J. Herigon, MD, MPH, MBI
  Findings from this review were presented with the question originator and J. Markham, MD, MSc, F. Turcotte, MD, MPH, FAAP, S. Bolger Theut, DO, M. Dannenberg, MD, A. Burns, PharmD, BCPPS, and R. Rolf on December 12, 2023.
Medical Librarian Responsible for the Search Strategy
  K. Swaggart, MLIS, AHIP
EBP Team or EBP Scholars Responsible for Analyzing the Literature
  A. Randall, MHA, RRT, RRT-ACCS, RRT-NPS, C-NPT, CPPS
EBP Medical Director Responsible for Reviewing the Literature
  T. Glenski, MD, MSHA, FASA
EBP Team Member Responsible for Reviewing, Synthesizing, and Developing this Document
  M. Gripka, MT (ASCP) SM

References

Barratt, S., Bielicki, J. A., Dunn, D., Faust, S. N., Finn, A., Harper, L., ... & Sharland, M. (2021). Amoxicillin duration and dose for community-acquired pneumonia in children: the CAP-IT factorial non-inferiority RCT. Health Technology Assessment, 25(60).

Bielicki, J. A., Stöhr, W., Barratt, S., Dunn, D., Naufal, N., Roland, D., ... & Keers, S. (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, 326(17), 1713-1724. doi:10.1001/jama.2021.17843

Bradley, J. S., Byington, C. L., Shah, S. S., Alverson, B., Carter, E. R., Harrison, C., ... & Swanson, J. T. (2011). The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clinical infectious diseases, 53*(7), e25-e76.

Guyatt, G. H., Oxman, A. D., Vist, G. E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., & Schünemann, H. J. (2008). GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Bmj, 336(7650), 924-926. doi:10.1136/bmj.39489.470347.AD

Higgins, J. P. T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J., Welch, V.A. (editors). (2022). *Cochrane Handbook for Systematic Reviews of Interventions [updated February 2022]* (Version 6.3): Cochrane, 2022. Available from www.training.cochrane.org/handbook. *Review Manager is a Cochrane Collaborative computer program used to assess the study characteristics.*

ISCAP Study Group. (2004). Three day versus five day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomised controlled trial. *Bmj, 328*(7443), 791.

Kuitunen, I., Jääskeläinen, J., Korppi, M., & Renko, M. (2023). Antibiotic treatment duration for community-acquired pneumonia in outpatient children in high-income countries—a systematic review and meta-analysis. Clinical Infectious Diseases, 76(3), e1123-e1128.

Li, Q., Zhou, Q., Florez, I. D., Mathew, J. L., Shang, L., Zhang, G., ... & Chen, Y. (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. https://doi.org/10.1001/jamapediatrics.2022.4123.

Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews, 5*(1), 210. doi:10.1186/s13643-016-0384-4 *Rayyan is a web-based software used for the initial screening of titles and / or abstracts for this analysis.*

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... & Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. International journal of surgery, 88, 105906. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicts the process in which literature is searched, screened, and eligibility criteria is applied. For more information, visit www.prisma-statement.org.

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Appendix

Table 2. Summary of Findings Table

QUESTION

In pediatric patients with uncomplicated community-acquired pneumonia (CAP), is 3 days of antibiotic treatment noninferior to a longer duration for clinical cure?	
POPULATION:	Pediatric patients with uncomplicated community acquired pneumonia (CAP)
INTERVENTION:	Shorter course antibiotic treatment (3 – 5 days)
COMPARISON:	Longer course antibiotic treatment (7 – 10 days)
MAIN OUTCOMES:	Treatment failure

ASSESSMENT

Certainty of evidence		
What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ● Moderate ○ High ○ No included studies	From the systematic review by Li et al. (2022): Eight studies reported treatment failure (N = 10,662). Treatment failure occurred in 12.8% of patients receiving short course treatment and in 12.6% of patients receiving long course treatment (RR 1.01, 95% CI [0.92, 1.12], p = .84). A 3-day course was noninferior to a 5-day course (RR 1.01, 95% CI [0.91, 1.12], p = .81) and a 5-day course was noninferior to a 10-day course (RR 0.87, 95% CI [0.50, 1.53], p = .64). The authors found the quality of evidence to be high for the outcome of treatment failure for all patients combined and for the subgroup of patients aged 2-59 months. However, for the subgroup of patients aged 5-10 years the quality of the evidence was low due to very serious imprecision due to the wide confidence interval of the result and small sample size of results.	

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Cost effectiveness		
Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ● Varies ○ No included studies	One study (ISCAP, 2004) found lower mean direct medical costs in the 3-day treatment group ($1100) vs. the 5-day treatment group ($1250).	The cost difference of short vs. long doses of antibiotics is minimal. The utilization of urgent care/ED for follow-up visits when the patient does not have a primary care provider varies. There may be a cost and utilization of resources associated with treatment of adverse effects attributed to longer doses of antibiotics.
Equity		
What would be the impact of the intervention on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know		The following may affect the equity of antibiotic treatment duration: cost of treatment and follow-up, patient adherence to treatment, and the patient's ability to follow-up with primary care provider.

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Acceptability Is the intervention acceptable to key stakeholders (including patients and families)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		Shorter course is more ideal for patients and families experiencing difficulties administering antibiotics due to patient resistance.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		This change will require education of providers. Adding a statement in the electronic health record (EHR) will facilitate implementation.

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TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	●

CONCLUSIONS

Recommendation
For patients with uncomplicated, mild, or moderate CAP, a strong recommendation is made for a shorter course of antibiotic treatment (3-5 days) for patients $\leq$ 5 years of age.

Subgroup considerations
Considerations for longer antibiotic treatment (5 – 7 days) should be made for hospitalized patients with CAP or patients ≥ 5 years of age. Data on shorter courses for hospitalized children or children > 5 years old are not as robust. Five days is generally sufficient in most cases of uncomplicated CAP.

Implementation considerations
Treatment recommendations will be added to the order set in the electronic health record and the Antimicrobial Stewardship Program (ASP) Outpatient Handbook.

Monitoring and evaluation
Antibiotic usage is monitored by ASP and can be monitored specifically for patients with CAP. The return visit rate to the ED and Urgent Care Clinics can be monitored for patients with CAP.

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Critically Appraised Topic (CAT):
Community Acquired Pneumonia Antibiotic Duration

Design	Quantitative Synthesis (meta-analysis)
Objective	To determine whether a shorter course of antibiotics was noninferior to a longer course for childhood non-severe Community Acquired Pneumonia (CAP)

Methods	**Criteria for considering studies for this review**
	• **Types of studies:** Randomized clinical trials
	• **Participants:** Children (less than 18 years of age)
	• **Target Condition(s):** CAP, non-severe
	
	Search methods for identification of studies
	• **Electronic databases searched:** MEDLINE (via PubMed), Embase, Web of Science, the Cochrane Library, China Biology Medicine, China NationalvKnowledge Infrastructure, and the WanFangData databases for eligible studies from inception to March 31, 2022, without language restrictions. Searches of ClinicalTrials.gov, The World Health Organization International Clinical Trial Registry Platform, and Google.com were also included.
	• **Search strategy employed:**
	   ○ MeSH terms used (pneumonia OR anti-bacterial agents OR beta-lactams OR penicillins OR ampicillin OR amoxicillin OR cephalosporins OR macrolides OR azithromycin OR sulfamethoxazole OR fluoroquinolones OR infant OR child OR pediatric OR adolescent)
	   ○ Keyword search for title/abstract, topic, and keyword in English and Chinese.
	   ○ No language limit applied
	   ○ Translation was performed when necessary
	• **Searching other resources (such as reference lists):** Searches were supplemented by hand-searching the reference lists of the included publications and previous meta-analyses. Described in supplemental Table 2.
	
	Data collection and analysis
	• **Inclusion criteria:**
	   ○ Randomized clinical trials comparing a shorter course (e.g., 3 days vs. 5-10 days and 5 days vs. 7-10 days) with a longer course of therapy using the same oral antibiotic for children (<18 years) with non-severe CAP.
	   ○ CAP was defined as pneumonia acquired outside of the hospital.
	   ○ Non-severe CAP was defined as the absence of any general danger signs of CAP (e.g., lethargy, unconsciousness, seizures, or inability to drink) and not requiring referral or injection therapy

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- **Exclusion criteria:**
  - Trials including only neonates, in which treatment groups received different antibiotics even if one group received a shorter course (e.g., azithromycin for 3 days vs cotrimoxazole for 5 days) or different doses of antibiotics (e.g., standard vs. double dose of amoxicillin)
  - Publications not presenting research findings (e.g., narrative reviews, protocols, opinions, editorials, and reports)
- **Population:** Less than 18 years of age
- **Setting:** Not specifically reported
- **Study Design:** RCTs
- **Data collection process:**
  - Two groups of investigators extracted data independently
  - Data from each study were tabulated and checked by a third investigator before analysis
  - Data collected included: age, sex, and country; diagnostic criteria, as well as classification and infection types of pneumonia; type, dose, frequency, and duration of antibiotics; length of follow-up; and outcomes
- **Assessment of the certainty of the evidence-**
  - Two reviews independently assessed the risk of bias with the Cochrane Risk of Bias tool. The risk of bias was classified as low, high, or unclear for each study.
  - Disagreements in these assessments were resolved by a third investigator.
- **Data Synthesis (what statistical plan do the authors establish a priori):** Random-effects models were used to pool the data, which were analyzed from April 15, 2022 to May 15, 2022
  - Dichotomous outcomes: data are presented as pooled risk ratios (RRs) and 95% CI. To facilitate interpretability, risk differences (RDs) were presented according to the probability of achieving the noninferiority margin.
  - Continuous variables are presented as mean differences with 95% CI
  - Sensitivity analysis to study the association of different definitions of pneumonia and treatment failure with the results by excluding one trial for every analysis
  - Small study effects were assessed by the Egger test, 21 with 2-sided P-values; the threshold for significance was .05. Data analyses with Stata, version 15.0 (StataCorp), and RevMan, version 5.4 (Nordic Cochrane Center, Cochrane Collaboration)
  - **Overall Effect Size (just state what is being used in the study)**
    - **Odds Ratio**
    - **Relative Risk**
    - **CI** (95% CI)
  - **Heterogeneity.** Heterogeneity was assessed with the I^2 statistic, and the values above 50% suggested substantial statistical heterogeneity

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Results	**Study Selection (actual results/data)**
	Number of articles identified: *N* = 7,978
	Full-text articles assessed for eligibility: *n* = 34
	o **Studies included in qualitative synthesis:** *n* = 9
	Synthesis of quality of evidence (strength of evidence):
	• Eight studies had adequate randomization, allocation concealment, and complete outcome data and were free from selective outcome reporting and other biases
	• Seven studies had adequate blinding of the participants and researchers
	• One study had insufficient information for judgment to be made
	Synthesis of quantitative evidence:
	• 3 days vs. 5 days (four studies)
	o For the outcome of treatment failure (*RR* = 1.01, 95% CI [0.91 – 1.12], *p* = .81
	o For the outcome of relapse (*RD* = 0, 95% CI [-0 – 0.01], *p* = .58
	• 3 days vs. 7 days (one study)
	o For the outcome of treatment failure (*RR* = 1.01, 95% CI [0.7 – 1.46], *p* = .96
	• 3 days vs. 10 days (one study)
	o For the outcome of treatment failure (*RR* = 6.55, 95% CI [0.41 – 105.1], *p* = .18
	• 5 days vs. 10 days (three studies)
	o For the outcome of treatment failure (*RR* = 0.87, 95% CI [0.98 – 1.27], *p* = .64
	o For the outcome of relapse (*RD* = -0.01, 95% CI [-0.08 – 0.06], *p* = .77
	• For the outcome of relapse (*RR* = 1.12, 95% CI [0.94 – 1.34] (six studies)
	• For the outcome of any serious adverse event (*RR* = 1.29, 95% CI [0.75 – 2.22] (three studies)
	• For the outcome of antimicrobial resistance
	o Short-Course Outpatient Therapy of Community-Acquired Pneumonia trial, the median number of β-lactamase resistance genes per prokaryotic cell during days 19 to 25 was significantly lower during the 5-day treatment compared with the 10-day treatment (0.55 [range, 0.18-1.24] vs. 0.60 [range, 0.21-2.45])
	o Community-Acquired Pneumonia: a randomized controlled (CAP-IT) trial, no significant differences in day 28 pneumococcal penicillin nonsusceptibility (14 of 205 vs. 7 of 232) or day 28 pneumococcal amoxicillin resistance or nonsusceptibility (2 of 205 vs. 2 of 232) between 3-day and 7-day treatments
	o INDIACLEN Short Course Amoxicillin Pneumonia Study -(ISCAP) reported that the proportion of *Streptococcus pneumoniae* isolates resistant to cotrimoxazole on day 14 were significantly lower with 3-day compared with 5-day treatment (66.7% vs 78.2%)
	o Kartasasmita and Saha found no significant difference in day 15 cotrimoxazole-resistant S. pneumoniae (61.5% vs 64.1%) between 3-day vs 5-day treatment

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	- For the outcome of absenteeism (one study)
	  - Caregiver work absenteeism was significantly lower in the 5-day group than in the 10-day group (incident rate ratio, 0.74; 95%CI [0.65-0.84])
	  - Child absenteeism was similar in the groups (incident rate ratio, 0.95; 95% CI [0.71-1.27])
	- For the outcome of cost, mean direct medical costs of treating 1000 cases of non-severe pneumonia were lower in the 3-day treatment group ($1100) than the 5-day treatment group ($1250) (one study)
	  - **Overall Effect Size**
	    - **Relative Risk** (0.11 - 105.1), dependent upon comparison and outcome
	      - For overall shorter course vs. longer course: *RR* = 1.01 95% CI [0.92, 1.11] (eight studies, *n* = 10,662)
	  - **Heterogeneity**
	    - Treatment failure: $t^2 = 0.0$; $\chi2 = 3.68$, df = 7 (*p* = .82); $I^2 = 0\%$
	    - Relapse: $t^2 = 0.0$; $\chi2 = 1.43$, df = 5 (*p* = .92); $I^2 = 0\%$

Discussion	**Summary of evidence**
	- A shorter course of oral antibiotics was non-inferior to a longer course with respect to treatment failure for children with CAP
	  - In the subgroup analysis, noninferiority was met for children aged 2 to 59 months but not met for children older than 5 years
	  - A 3-day course of antibiotic treatment was non-inferior to a 5-day course for the outcome of treatment failure and a 5-day course was non-inferior to a 10-day course
	  - Noninferiority continued to be met in other subgroups, except the comparison between a 3-day and a 10-day course
	- A shorter course of oral antibiotics was non-inferior to a longer course with respect to relapse
	- No differences between the interventions in the risk of other nonserious events or any serious adverse events
	  - Risks of gastroenteritis and rash were significantly lower in short-course groups compared with long-course groups
	- Caregiver absenteeism was higher in the longer-course treatment
	- Mean direct medical costs were lower in the shorter-course treatment
	Limitations
	- Multiple infection types included, and it is possible that the optimal duration of antibiotics differs by different types
	- Microbiologic testing is not routinely performed in outpatient and inpatient settings
	- Neither chest radiographs nor inflammatory biomarkers can reliably discriminate among children with viral, atypical, and bacterial CAP
	- Definitions of pneumonia and treatment failure varied across studies, which may have led to heterogeneity in results

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	• The definition of non-severe CAP was non-specific and open to interpretation. • Long-term outcomes not analyzed, due to lack of data
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