National Institute for Health and Care Excellence

Final

Meningitis (bacterial) and meningococcal disease: recognition, diagnosis and management

[D1] Evidence reviews for antibiotics for bacterial meningitis before or in the absence of identifying causative infecting organism in younger infants

NICE guideline NG240

Evidence review underpinning recommendations 1.6.4 to 1.6.9 and 1.6.16 in the NICE guideline

March 2024

Final

This evidence review was developed by NICE

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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.

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Antibiotics for bacterial meningitis before or in the absence of identifying causative infecting organism in younger infants

Review question

What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants (excluding neonates) before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

Introduction

Bacterial meningitis is a rare but serious infection. In younger infants, the range of bacterial aetiologies differs from those seen in older infants, children and most adults.

The aim of this review is to establish the appropriate empirical antibiotic treatment regimen(s) that are effective in treating suspected bacterial meningitis in younger infants, before, or in the absence of identifying, the causative infecting organism.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Younger infants (>28 days to ≤3 months of age) with suspected bacterial meningitis
Intervention	Antibiotic agent of interest: Amoxicillin, Ampicillin, Benzylpenicillin sodium, Cefotaxime, Ceftriaxone, Gentamicin In cases of severe beta-lactam allergy: Fluoroquinolones (all licensed in the UK), Chloramphenicol
Comparison	**Stage 1 (all antibiotic agents of interest):** Comparison: • Amoxicillin or ampicillin plus cefotaxime or ceftriaxone vs amoxicillin or ampicillin plus gentamicin • Amoxicillin or ampicillin plus cefotaxime or ceftriaxone vs benzylpenicillin sodium plus gentamicin • Amoxicillin or ampicillin plus gentamicin vs benzylpencillin sodium plus gentamicin • Amoxicillin or ampicillin plus gentamicin vs cefotaxime or ceftriaxone alone • Benzylpenicillin sodium plus gentamicin vs cefotaxime or ceftriaxone alone • Amoxicillin or ampicillin plus cefotaxime or ceftriaxone vs cefotaxime or ceftriaxone alone In cases of severe beta-lactam allergy: • Chloramphenicol vs fluoroquinolones **Stage 2 (antibiotic agents identified during stage 1 as most effective/for use where there are contraindications)** Comparisons: • Antibiotic agent A – Dose A vs Antibiotic agent A – Dose B • Antibiotic agent A – Duration of administration A vs Antibiotic agent A – Duration of administration B

	• Antibiotic agent A – Short infusion vs Antibiotic agent A – Extended infusion
Outcome	**Critical** • All-cause mortality (measured up to 1 year after discharge) • Any long-term neurological impairment (defined as any motor deficits, sensory deficits [excluding hearing impairment], cognitive deficits*, or behavioural deficits*; measured from discharge up to 1 year after discharge) • Severe developmental delay (defined as score of >2 SD below normal on validated assessment scales, or MDI or PDI <70 on Bayleys assessment scale, or inability to assign a score due to cerebral palsy or severity of cognitive delay; measured at the oldest age reported unless there is substantially more data available at a younger age) **Important** • Diagnosis of epilepsy or occurrence of seizures during hospitalisation • Hearing impairment (defined as any level of hearing impairment; measured from discharge up to 1 year after discharge) • Functional impairment (measured by any validated scale at any time point) • Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant *For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age.

MDI: mental development index; PDI: psychomotor development index; SD: standard deviation

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

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

Effectiveness evidence

Included studies

A systematic review of the literature was conducted but no studies were identified which were applicable to this review question.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix J.

Summary of included studies

No studies were identified which were applicable to this review question (and so there are no evidence tables in Appendix D). No meta-analysis was conducted for this review (and so there are no forest plots in Appendix E).

Summary of the evidence

No studies were identified which were applicable to this review question (and so there are no GRADE tables in Appendix F).

Economic evidence

Included studies

A single economic search was undertaken for all topics included in the scope of this guideline, but no economic studies were identified which were applicable to this review question.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation. This was because the choice of antibiotics in this population is quite limited, and the costs are generally similar and relatively inexpensive. Furthermore, local patterns of antibiotic resistance and allergies can also constrain the decision set.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Bacterial meningitis is associated with high rates of mortality and morbidity, and antibiotics are the mainstay of treatment for bacterial meningitis. Therefore, all-cause mortality and long-term neurological impairment were prioritised as critical outcomes because of the severity of these outcomes. Severe developmental delay was prioritised as a critical outcome while functional impairment was chosen as an important outcome because severe developmental delay is a more relevant and important outcome in babies and children.

In addition to functional impairment, epilepsy or seizures, hearing impairment and serious intervention-related adverse effects were chosen as important outcomes because these outcomes are relatively common after bacterial meningitis and may be related to antibiotic therapy.

The quality of the evidence

No studies were identified which were applicable to this review question.

Benefits and harms

No evidence was identified for the effectiveness of antibiotic treatment regimens in young babies (aged 29 days to 3 months) with suspected bacterial meningitis. Therefore, the committee made recommendations based on their clinical knowledge and experience.

The committee discussed common infective organisms (for example, Escherichia coli, Streptococcus pneumoniae and Neisseria meningitidis) in this age group and agreed to recommend intravenous ceftriaxone for suspected bacterial meningitis in young babies in line with the British National Formulary for Children (BNFC) (Paediatric Formulary Committee 2022). The committee were aware that insufficient dose can increase the risk of treatment failure and antibiotic resistance; therefore, they agreed to use the maximum dose recommended by the BNFC or follow local antimicrobial guidance. The committee highlighted the practical and resource-use advantages associated with ceftriaxone because it has a broad spectrum of activity, and the long half-life means that it can be given only once a day. The committee acknowledged some concerns with once daily administration in that a

second dose might need to be delayed if the first dose of ceftriaxone was administered outside of routine working hours; however, they were aware that a second dose can be given earlier, to shift the administration time, if there is a minimum of 12 hours between doses (Gbesemete 2019).

The committee discussed some reasons why in clinical practice (particularly in intensive care units) cefotaxime might be given instead of ceftriaxone. For instance, to minimise the time that intravenous lines are being used for administering antibiotics, which might be needed for other medications, due to ceftriaxone typically being infused over 30 minutes intravenous and cefotaxime being given as a bolus. However, the committee agreed that this practice is not necessary, as ceftriaxone can be given as bolus. Sometimes there may be a reaction (for example, vomit reflex) if ceftriaxone is administered too quickly, but in the committee's experience this is relatively rare, which was supported by a recent study (Patel 2021). The committee agreed that ceftriaxone should be given as first-line treatment for suspected bacterial meningitis when the causative organism has not been identified, unless contraindicated (as outlined in the BNFC) in which case cefotaxime can be considered.

The committee highlighted the importance of considering the possibility of a cephalosporin-resistant pneumococcus causing bacterial meningitis. The committee were aware that the previous NICE guideline on meningitis (NICE 2010) recommended to treat people who have travelled outside the UK or had prolonged or multiple exposure to antibiotics within the last 3 months with vancomycin (in addition to the cephalosporin). However, they discussed that practice has changed since the previous NICE guideline and agreed that changes to this recommendation were required. Firstly, the committee were aware that current practice is to use rifampicin or linezolid in addition to a cephalosporin where the cephalosporin itself might be insufficient due to resistance. However, the committee highlighted that there is not enough evidence about the effectiveness and safety of rifampicin or linezolid in suspected (or confirmed) cephalosporin resistant bacterial meningitis to support recommending them. Therefore, the committee recommended that, clinicians should seek advice from an infection specialist (a microbiologist or infectious diseases specialist) for all cases of bacterial meningitis, but this was particularly important if cephalosporin resistance is suspected in young babies who have recently travelled abroad. Secondly, the committee noted that the evidence used to inform the recommendation about prolonged or multiple exposure to antibiotics in the previous guideline came from Canada (Vanderkooi 2005), which has a higher prevalence of cephalosporin resistance than the UK. The committee discussed that there was insufficient evidence that prolonged or multiple exposure to antibiotics on an individual level causes people to be colonised with resistant organisms. Rather, the committee agreed that it is antibiotic use at a population level that contributes to cephalosporin resistant bacteria. Therefore, the committee agreed that the evidence did not warrant recommending different treatment for these people. Moreover, the committee noted that, in their experience, such people are not currently treated differently. The committee were aware that Enterobacterales (coliforms) are relatively common in young babies and tend to be resistant to cephalosporins. Therefore, the committee agreed that alternative antibiotics may be needed for young babies colonised with cephalosporin-resistant Enterobacterales (coliforms) who develop bacterial meningitis. In the absence of evidence on the effectiveness of antibiotic regimens in this group, the committee recommended that infection specialist advice is sought where cephalosporin resistance is suspected.

There was no evidence found on antibiotic use for suspected bacterial meningitis in young babies with an antibiotic allergy, but the committee agreed it was important to make a recommendation for this population. Based on their knowledge and experience, the committee agreed that cephalosporin-induced anaphylaxis is rare, and the risk-benefit balance of cephalosporin relative to chloramphenicol is favourable in the majority of people with non-severe allergy. Therefore, the committee agreed that clinicians should seek information about the nature of the allergy and advice from an infection specialist before making a treatment decision. The committee acknowledged that it is important that treatment is not delayed; however, they agreed that information about the nature of allergy is often

readily available from the patient's parents or guardians. The committee agreed that ceftriaxone should still be considered if the nature of the allergic reaction they get is not severe, in accordance with the first line treatment recommended above. However, if the allergic reaction is severe, alternatives to ceftriaxone will be needed. The committee discussed that chloramphenicol is commonly used in the case of severe beta-lactam allergy, but they were aware that its spectrum of activity does not cover Enterobacterales (coliforms). However, the committee acknowledged that meningitis caused by Enterobacterales (coliforms) is rare and typically happens only in the first weeks of life where you would not see an anaphylactic reaction, so in practice this situation would rarely occur. For young babies with severe allergic reactions, the committee recommended chloramphenicol.

The committee noted that listeria is not susceptible to ceftriaxone or cefotaxime based on their clinical knowledge and experience, and whilst listeria is most common in older adults, risk factors for listeria should also be considered in young babies. The committee were aware that amoxicillin is recommended by the BNFC (Paediatric Formulary Committee 2022) for meningitis caused by listeria monocytogenes (in combination with another antibiotic). Therefore, the committee recommended that intravenous amoxicillin should be part of the first line treatment described above for young babies with risk factors for listeria.

The committee agreed it was important to make a recommendation about appropriate antibiotic treatment for young babies with risk factors for Listeria monocytogenes and a history of antibiotic allergy. The committee were aware that current practice would be to consider the use of co-trimoxazole for both severe and non-severe allergic reactions, rather than amoxicillin, in addition to the first line treatment recommended above for people with a history of antibiotic allergy and, in line with current practice, recommended co-trimoxazole (in addition to cephalosporin for non-severe allergy or in addition to chloramphenicol for severe allergy) for young babies with an antibiotic allergy who have risk factors for Listeria monocytogenes.

The committee were aware that the previous NICE guideline on bacterial meningitis made recommendations about the use of antibiotics for herpes simplex encephalitis. The committee acknowledged that this condition was not included in the scope for the current guideline. The committee were aware that prescribing aciclovir has become routine practice in cases of suspected bacterial meningitis (Hagen 2020) and were concerned about the overuse of aciclovir. Therefore, the committee made a recommendation to clarify that aciclovir should only be given when herpes simplex encephalitis is strongly suspected.

The committee agreed that there should be a recommendation about duration of antibiotic treatment. The committee were aware that the results of confirmatory tests could be available within 48 to 72 hours and recommended that empirical antibiotic treatment should be continued until results suggest an alternative treatment is needed, or there is an alternative diagnosis, which is in line with current practice. The committee agreed that it was necessary to specify a duration of antibiotic treatment for cases where the CSF parameters are consistent with bacterial meningitis, but the blood culture and whole-blood diagnostic PCR are negative. The committee acknowledged that different durations of antibiotic therapy are needed for different causative organisms. Given that Streptococcus pneumoniae and Neisseria meningitidis are common causes of bacterial meningitis in this age group, the committee agreed that the duration of antibiotic treatment should be consistent with the treatment recommended for these causative organisms and as 10 days is the longer duration of treatment prior to review (recommended for Streptococcus pneumoniae meningitis) this was considered the most appropriate default duration to recommend in culture negative cases. The committee also agreed that advice from an infection specialist should be sought if young babies have not recovered after 10 days.

Cost effectiveness and resource use

This review question was not prioritised for economic analysis and therefore the committee made a qualitative assessment of the likely cost-effectiveness of their recommendations. No evidence was identified for the effectiveness of antibiotic treatment regimens in young babies. The committee reasoned that it would be cost-effective to recommend ceftriaxone for young babies, as it is potentially less resource intensive as it can be given once a day compared to cefotaxime which is given 3 times daily. As these recommendations were in line with current NHS practice and updates made to the BNFC since the previous guideline, no significant resource impact is anticipated.

The committee also made recommendations outlining when infection specialist advice should be sought reflecting their view that the cost-effective choice of antibiotic would depend on the specific individualised characteristics of the presenting young baby, such as in cases of suspected or confirmed cephalosporin resistant bacterial meningitis.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.6.4 to 1.6.9 and 1.6.16. Other evidence supporting these recommendations can be found in evidence reviews on antibiotic regimens for bacterial meningitis before or in the absence of identifying causative infecting organism in older infants and children, and adults (see evidence reviews D2 and D3) and for specific causative organisms (see evidence reviews E1 to E6).

References – included studies

Effectiveness

No studies were identified which were applicable to this review question.

Economic

No studies were identified which were applicable to this review question.

Other

Gbesemete 2019

Gbesemete, D., Faust, S. (2019). Prescribing in infection: antibacterials. In. Barker, C., Turner, M., Sharland, M. (Eds.) Prescribing Medicines for Children: From drug development to practical administration, Pharmaceutical Press, London: UK

Hagen 2020

Hagen, A., Eichinger, A., Meyer-Buehn, M. et al. (2020). Comparison of antibiotic and acyclovir usage before and after the implementation of an on-site FilmArray meningitis/ encephalitis panel in an academic tertiary pediatric hospital: a retrospective observational study, BMC Pediatrics 20(1), 56

NICE 2010

National Institute for Health and Care Excellence (2010). Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management. Available at: https://www.nice.org.uk/guidance/cg102 [Accessed 04/04/2022]

Paediatric Formulary Committee 2022

Paediatric Formulary Committee. BNF for Children (online). London: BMJ Group, Pharmaceutical Press, and RCPCH Publications. Available at: http://www.medicinescomplete.com [Accessed 29/03/2022]

Patel 2021

Patel, S., Green. H., Gray, J., Rutter, M., Bevan, A., Hand, K., Jones, C. E., Faust, S. N. (2021). Evaluating Ceftriaxone 80 mg/kg Administration by Rapid Intravenous Infusion—A Clinical Service Evaluation. The Pediatric Infectious Disease Journal, 40(2), 128-129

Vanderkooi 2005

Vanderkooi, O. G., Low, E. D., Green, K. et al. (2005). Predicting antimicrobial resistance in invasive pneumococcal infections, Clinical Infectious Diseases 40(9), 1288-1297

Appendices

Appendix A Review protocols

Review protocol for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

Table 2: Review protocol

Field	Content
PROSPERO registration number	CRD42021234208
Review title	Antibiotics for bacterial meningitis before or in the absence of identifying causative infecting organism in younger infants
Review question	What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants (excluding neonates) before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?
Objective	This review aims to find out what is the optimal antibiotic treatment regimen in improving outcomes for younger infants with suspected bacterial meningitis before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism
Searches	The following databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Database of Systematic Reviews (CDSR) Embase MEDLINE Searches will be restricted by: Date limitations: 1980 English language Human studies

Field	Content
	The full search strategies for MEDLINE database will be published in the final review. For each search, the principal database search strategy is quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist.
Condition or domain being studied	Suspected bacterial meningitis
Population	Inclusion: Younger infants (defined as >28 days to ≤3 months old) with suspected bacterial meningitis Exclusion: People: • with known immunodeficiency. • who have brain tumours, pre-existing hydrocephalus, intracranial shunts, previous neurosurgical procedures, or known cranial or spinal anomalies that increase the risk of bacterial meningitis. • with confirmed viral meningitis or viral encephalitis. • with confirmed tuberculous meningitis. • with confirmed fungal meningitis.
Intervention/Exposure/Test	Antibiotic agent of interest: • Amoxicillin • Ampicillin • Benzylpenicillin sodium • Cefotaxime • Ceftriaxone • Gentamicin In cases of severe beta-lactam allergy: • Fluoroquinolones (all licensed in the UK)

Field	Content
	• Chloramphenicol
Comparator/Reference standard/Confounding factors	Stage 1 (all antibiotic agents of interest): Comparison: • Amoxicillin or ampicillin plus cefotaxime or ceftriaxone vs amoxicillin or ampicillin plus gentamicin • Amoxicillin or ampicillin plus cefotaxime or ceftriaxone vs benzylpenicillin sodium plus gentamicin • Amoxicillin or ampicillin plus gentamicin vs benzylpencillin sodium plus gentamicin • Amoxicillin or ampicillin plus gentamicin vs cefotaxime or ceftriaxone alone • Benzylpenicillin sodium plus gentamicin vs cefotaxime or ceftriaxone alone • Amoxicillin or ampicillin plus cefotaxime or ceftriaxone vs cefotaxime or ceftriaxone alone In cases of severe beta-lactam allergy: • Chloramphenicol vs fluoroquinolones Stage 2 (antibiotic agents identified during stage 1 as most effective/for use where there are contraindications) Comparisons: 1. Antibiotic agent A – Dose A vs Antibiotic agent A – Dose B 2. Antibiotic agent A – Duration of administration A vs Antibiotic agent A – Duration of administration B 3. Antibiotic agent A – Short infusion vs Antibiotic agent A – Extended infusion
Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • RCTs • If insufficient RCTs: prospective cohort studies • If insufficient prospective cohort studies: retrospective cohort studies Non-randomised studies will be downgraded for risk of bias if they do not adequately

Field	Content
	adjust for the following covariates, but will not be excluded for this reason: • Co-morbidity • Severity of infection at presentation (including sepsis) • Antibiotics administered pre or post lumbar puncture • Infective organisms Exclude: • Conference abstracts
Other exclusion criteria	Cohort studies from low income countries. Studies conducted prior to 1980 as currently used antibiotics were not in common usage prior to this date. Studies published not in English-language
Context	This guidance will fully update the following: Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (CG102)
Primary outcomes (critical outcomes)	• All-cause mortality (measured up to 1 year after discharge) • Any long-term neurological impairment (defined as any motor deficits, sensory deficits [excluding hearing impairment], cognitive deficits*, or behavioural deficits*; measured from discharge up to 1 year after discharge) • Severe developmental delay (defined as score of >2 SD below normal on validated assessment scales, or MDI or PDI <70 on Bayleys assessment scale, or inability to assign a score due to cerebral palsy or severity of cognitive delay; measured at the oldest age reported unless there is substantially more data available at a younger age) *For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age.
Secondary outcomes (important outcomes)	• Diagnosis of epilepsy or occurrence of seizures during hospitalisation • Hearing impairment (defined as any level of hearing impairment; measured from

Field	Content
	discharge up to 1 year after discharge) • Functional impairment (measured by any validated scale at any time point) • Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will not be undertaken for this question. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs and quasi-RCTs • Cochrane ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where multiple studies report on the same outcome for the same comparison, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios if possible or odds ratios when required (for example if only available in this form in included studies) for dichotomous

Field	Content
	outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed by visual inspection of the forest plots and consideration of the I2 statistic. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled if the random effects model does not adequately address heterogeneity. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences:** • All-cause mortality: statistical significance • Serious intervention-related adverse effects: statistical significance • Length of hospitalisation: 1 day • Validated scales: Published MIDs where available; if not GRADE default MIDs • All other outcomes: GRADE default MIDs
Analysis of sub-groups	No preplanned stratifications. Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes: Status of infective organism: • Before organism is identified • Absence of identified organism Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate

Field	Content			
	recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.			
Type and method of review	☒	Intervention		
	☐	Diagnostic		
	☐	Prognostic		
	☐	Qualitative		
	☐	Epidemiologic		
	☐	Service Delivery		
	☐	Other (please specify)		
Language	English			
Country	England			
Anticipated or actual start date	12/01/2021			
Anticipated completion date	07/12/2023			
Stage of review at time of this submission	Review stage		Started	Completed
	Preliminary searches		☑	☑
	Piloting of the study selection process		☑	☑
	Formal screening of search results against eligibility criteria		☑	☑
	Data extraction		☑	☑
	Risk of bias (quality) assessment		☑	☑
	Data analysis		☑	☑
Named contact	Named contact: National Guideline Alliance			

Field	Content
	Named contact e-mail: meningitis&meningococcal@nice.org.uk Organisational affiliation of the review: National Institute for Health and Care Excellence (NICE) and National Guideline Alliance
Review team members	National Guideline Alliance
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance which receives funding from NICE.
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10149.
Other registration details	None
Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021234208
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

Field	Content	
Keywords	Bacterial meningitis, antibiotic, anti-bacterial, mortality, impairments	
Details of existing review of same topic by same authors	None	
Current review status	☐	Ongoing
	☒	Completed but not published
	☐	Completed and published
	☐	Completed, published and being updated
	☐	Discontinued
Additional information	None	
Details of final publication	www.nice.org.uk	

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; GRADE: Grading of Recommendations Assessment, Development and Evaluation; MDI: mental development index; MEDLINE: Medical Literature Analysis and Retrieval System Online; MID: minimally important difference; NICE: National Institute for Health and Care Excellence; PDI: psychomotor development index; PRESS: Peer Review of Electronic Search Strategies; RCT: randomised controlled trial; RoB: risk of bias; ROBINS-I: risk of bias in non-randomised studies – of interventions; ROBIS: risk of bias in systematic reviews; SD: standard deviation

Appendix B Literature search strategies

Literature search strategies for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

Clinical Search

This was a combined search to cover both this review (D1) and D2, D3, E1, E2, E3, E4, E5, E6 and F1 on antibiotic regimens for bacterial meningitis (before or in the absence of identifying causative infecting organism and for specific causative organisms) and meningococcal disease.

Database(s): Medline & Embase (Multifile) – OVID interface
Embase Classic+Embase 1947 to 2022 November 09, **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to November 09, 2022
Date of last search: 10 November 2022
Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	Meningitis/ or Meningitis, Bacterial/ or Meningitis, Escherichia Coli/ or Meningitis, Haemophilus/ or Meningitis, Listeria/ or Meningitis, Meningococcal/ or Meningitis, Pneumococcal/ or Meningoencephalitis/
2	1 use ppez
3	meningitis/ or bacterial meningitis/ or haemophilus meningitis/ or hemophilus influenzae meningitis/ or listeria meningitis/ or meningococcal meningitis/ or pneumococcal meningitis/ or meningoencephalitis/
4	3 use emczd
5	((bacter* or infect*) adj3 (meningit* or meninges* or leptomeninges* or subarachnoid space?)).ti,ab.
6	(meningit* adj3 (e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon* or septic* or sepsis* or bacter?emi?)).ti,ab.
7	((e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon*) adj3 (septic* or sepsis* or bacter?emi?)).ti,ab.
8	(meningit* or mening?encephalitis*).ti,ab.
9	exp Neisseria meningitidis/ use ppez
10	neisseria meningitidis/ use emczd
11	(Neisseria* mening* or n mening*).ti,ab.
12	or/2,4-11
13	Meningococcal Infections/ use ppez
14	meningococcosis/ or meningococcemia/
15	14 use emczd
16	(meningococc* adj3 (sepsis* or septic* or toxic* or endotoxic* or disease? or infection?)).ti,ab.
17	(meningococcus* or meningococci* or meningococc?emi?).ti,ab.
18	or/13,15-17
19	exp Anti-Bacterial Agents/ or exp Penicillins/ or exp Cephalosporins/ or exp Cefotaxime/ or exp Amoxicillin/ or exp Ampicillin/
20	19 use ppez
21	exp antibiotic agent/ or antibiotic therapy/ or exp penicillin derivative/ or exp cephalosporin derivative/
22	21 use emczd
23	(anti?biotic* or anti?bacterial* or anti?biotherap*).ti,ab.
24	(empiric* adj2 (therap* or treatment*)).ti,ab.
25	(abbocillin or adimicin or alcomicin or alpen or amblosin or amcill or amfipen or aminobenzylpenicillin* or aminoglycosid* or amox?cillin* or amoxil* or ampicillin* or ancef or anticepim or apogen or axepim* or ayercillin or azithrom?cin* or benzo?penicillin* or benzyl?penicillin* or bicillin or binotal or biomox or bmy 28142 or bmy?28142 or bristagen or bristamox or carbapenem* or cedax or ceftazidim* or cefatriaxon* or cefepim* or cefixim* or cefizox or cefobid* or cefotan or cefotaxim* or ceftaroline* or ceftin or ceftolozane* or ceftriaxon* or ceftriazon* or cefuroxim* or cefzil or cepazin* or cephalosporin* or cephotaxim* or cephuroxim* or cepim?x or chloramphenicol* or ciprofloxacin* or claforan or clamoxyl or clarithromycin* or clindamycin* or colistin* or compocillin or cosmopen or cotrimoxazol* or co trimoxazol* or crysticillin or delafloxacin* or deripen or dexamethasone or diatracin or doktacillin or duricef or elobact or erythromycin* or flucloxacillin* or fluoroquinolon* or fosfomycin* or gelacillin or gentam?cin* or gent?mycin* or gentamyl* or gentamytrex or gentaplus or gentarad or gentaso* or gentasporin or gentatrim or gent?cin* or gent?cyn* or geocillin* or geomycin* or glycopeptid* or guicitrin* or hexam?cin* or hiconcil or histocillin or ibiamox or imacillin or jenamicin or kefurox or kefzol or klaforan or lendacin or levofloxacin* or linezolid* or longacef or longaceph or lyphocin

#	Searches
	or macrolide* or mandol or maxcef or maxipim* or mefoxin or megacillin or meropen* or miram?cin* or monocid or moxacin or moxifloxacin* or ofloxacin* or oftagen* or omnipen or optigen* or pefloxacin* or penbritin* or penbrock or penicillin? or penicline or pentids or pentrex or pentrexl or pentrexyl or permapen or pfizerpen or polycillin or polymox or polymyxin*or primafen or principen or quinolon* or refobacin* or ribom?cin* or rifampicin or rifampin* or rocefalin or rocefin or rocephin* or roscillin or rufloxacin* or sagestam* or spectrobid or sulm?cin* or supen or tazobactam* or terram?cin* or tetracycline* or tobramycin* or totacillin or totapen or trimox or u?gencin* or ukapen or ultrabion or vamysin or vancam* or vanccostacin or vancin or vancom* or vancomycin* or vankom* or velosef or vetramox* or viccillin or voncon* or wycillin or zimox or zinacef or zin?at).mp.
26	or/20,22-25
27	(12 or 18) and 26
28	(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or placebo or randomi#ed or randomly or trial).ab.
29	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
30	meta-analysis/
31	meta-analysis as topic/
32	systematic review/
33	meta-analysis/
34	(meta analy* or metanaly* or metaanaly*).ti,ab.
35	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
36	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
37	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
38	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
39	(search* adj4 literature).ab.
40	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
41	cochrane.jw.
42	((pool* or combined) adj2 (data or trials or studies or results)).ab.
43	letter/
44	editorial/
45	news/
46	exp historical article/
47	Anecdotes as Topic/
48	comment/
49	case report/
50	(letter or comment*).ti.
51	43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
52	randomized controlled trial/ or random*.ti,ab.
53	51 not 52
54	animals/ not humans/
55	exp Animals, Laboratory/
56	exp Animal Experimentation/
57	exp Models, Animal/
58	exp Rodentia/
59	(rat or rats or mouse or mice).ti.
60	53 or 54 or 55 or 56 or 57 or 58 or 59
61	letter.pt. or letter/
62	note.pt.
63	editorial.pt.
64	case report/ or case study/
65	(letter or comment*).ti.
66	61 or 62 or 63 or 64 or 65
67	randomized controlled trial/ or random*.ti,ab.
68	66 not 67
69	animal/ not human/
70	nonhuman/
71	exp Animal Experiment/
72	exp Experimental Animal/
73	animal model/
74	exp Rodent/
75	(rat or rats or mouse or mice).ti.
76	68 or 69 or 70 or 71 or 72 or 73 or 74 or 75
77	60 use ppez
78	76 use emczd
79	77 or 78
80	28 use ppez
81	29 use emczd
82	80 or 81
83	(or/30-31,34,36-41) use ppez
84	(or/32-35,37-42) use emczd

#	Searches
85	83 or 84
86	27 not 79
87	limit 86 to English language
88	limit 87 to yr="1980 -Current"
89	limit 88 to (conference abstract or conference paper or conference review or conference proceeding) [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]
90	89 use emczd
91	88 not 90
92	82 or 85
93	91 and 92
94	91 not 93

Database(s): Cochrane Library – Wiley interface
Cochrane Database of Systematic Reviews, Issue 11 of 12, November 2022, **Cochrane Central Register of Controlled Trials**, Issue 11 of 12, November 2022
Date of last search: 10 November 2022

#	Searches
#1	MeSH descriptor: [Meningitis] this term only
#2	MeSH descriptor: [Meningitis, Bacterial] this term only
#3	MeSH descriptor: [Meningitis, Escherichia coli] this term only
#4	MeSH descriptor: [Meningitis, Haemophilus] this term only
#5	MeSH descriptor: [Meningitis, Listeria] this term only
#6	MeSH descriptor: [Meningitis, Meningococcal] this term only
#7	MeSH descriptor: [Meningitis, Pneumococcal] this term only
#8	MeSH descriptor: [Meningoencephalitis] this term only
#9	MeSH descriptor: [Neisseria meningitidis] explode all trees
#10	((bacter* or infect*) near/3 (mening* or leptomening* or subarachnoid space*)):ti,ab,kw
#11	(("e coli" or "escherichia coli" or haemophilus or hemophilus or hib or (h next influenz*) or listeria* or pneumococc* or (gram next negativ* next bacill*) or streptococc* or GBS or (s next pneumon*)) near/3 (septic* or sepsis* or bacteraemi* or bacteremi* or infect*)):ti,ab,kw
#12	(meningit* or mening?encephalitis* or (mening* next encephalitis*)).:ti,ab,kw
#13	((neisseria* next mening*) or (n next mening*)):ti,ab,kw
#14	MeSH descriptor: [Meningococcal Infections] this term only
#15	meningococc*:ti,ab,kw
#16	{or #1-#15}
#17	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#18	((antibiotic* or antibacterial* or antibiotherap* or "anti biotic*" or "anti bacterial*" or "anti biotherap*")):ti,ab,kw
#19	((empiric* near/2 (therap* or treatment*))):ti,ab,kw
#20	((abbocillin or adimicin or alcomicin or alpen or amblosin or amcill or amfipen or aminobenzylpenicillin* or aminoglycosid* or amox?cillin* or amoxil* or ampicillin* or ancef or anticepim or apogen or axepim* or ayercillin or azithrom?cin* or benzo?penicillin* or benzyl?penicillin* or bicillin or binotal or biomox or bmy 28142 or bmy?28142 or bristagen or bristamox or carbapenem* or cedax or ceftazidim* or cefatriaxon* or cefepim* or cefixim* or cefizox or cefobid* or cefotan or cefotaxim* or ceftaroline* or ceftin or ceftolozane* or ceftriaxon* or ceftriazon* or cefuroxim* or cefzil or cepazin* or cephalosporin* or cephotaxim* or cephuroxim* or cepim?x or chloramphenicol* or ciprofloxacin* or claforan or clamoxyl or clarithromycin* or clindamycin* or colistin* or compocillin or cosmopen or cotrimoxazol* or co trimoxazol* or crysticillin or delafloxacin* or deripen or dexamethasone or diatracin or doktacillin or duricef or elobact or erythromycin* or flucloxacillin* or fluoroquinolon* or fosfomycin* or gelacillin or gentam?cin* or gent?mycin* or gentamyl* or gentamytrex or gentaplus or gentarad or gentaso* or gentasporin or gentatrim or gent?cin* or gent?cyn* or geocillin* or geomycin* or glycopeptid* or guicitrin* or hexam?cin* or hiconcil or histocillin or ibiamox or imacillin or jenamicin or kefurox or kefzol or klaforan or lendacin or levofloxacin* or linezolid* or longacef or longaceph or lyphocin or macrolide* or mandol or maxcef or maxipim* or mefoxin or megacillin or meropen* or miram?cin* or monocid or moxacin or moxifloxacin* or ofloxacin* or oftagen* or omnipen or optigen* or pefloxacin* or penbritin* or penbrock or penicillin? or penicline or pentids or pentrex or pentrexl or pentrexyl or permapen or pfizerpen or polycillin or polymox or polymyxin*or primafen or principen or quinolon* or refobacin* or ribom?cin* or rifampicin or rifampin* or rocefalin or rocefin or rocephin* or roscillin or rufloxacin* or sagestam* or spectrobid or sulm?cin* or supen or tazobactam* or terram?cin* or tetracycline* or tobramycin* or totacillin or totapen or trimox or u?gencin* or ukapen or ultrabion or vamysin or vancam* or vanccostacin or vancin or vancom* or vancomycin* or vankom* or velosef or vetramox* or viccillin or voncon* or wycillin or zimox or zinacef or zin?at)):ti,ab,kw
#21	{or #17-#20}
#22	#16 and #21
#23	"conference":pt or (clinicaltrials or trialsearch):so
#24	#22 not #23

Database(s): Database of Abstracts of Reviews of Effects (DARE); HTA Database – CRD interface
Date of last search: 12 February 2021

#	Searches

#	Searches
1	MeSH DESCRIPTOR meningitis IN DARE,HTA
2	MeSH DESCRIPTOR meningitis, bacterial IN DARE,HTA
3	MeSH DESCRIPTOR Meningitis, Escherichia coli IN DARE,HTA
4	MeSH DESCRIPTOR Meningitis, Haemophilus IN DARE,HTA
5	MeSH DESCRIPTOR Meningitis, Listeria IN DARE,HTA
6	MeSH DESCRIPTOR Meningitis, Meningococcal IN DARE,HTA
7	MeSH DESCRIPTOR Meningitis, Pneumococcal IN DARE,HTA
8	MeSH DESCRIPTOR Meningoencephalitis IN DARE,HTA
9	MeSH DESCRIPTOR Meningococcal infections IN DARE,HTA
10	(((((bacter* or infect*) NEAR3 (meningit* or meninges* or leptomeninges* or "subarachnoid space*"))))) IN DARE, HTA
11	(meningit*) IN DARE, HTA
12	((((meningencephalitis* or meningoencephalitis*)))) IN DARE, HTA
13	((((meningococc* NEAR3 (sepsis* or septic* or toxic* or endotoxic* or disease or diseases or infection or infections))))) IN DARE, HTA
14	((((meningococcus* or meningococci* or meningococcaemia* or meningococcemia*)))) IN DARE, HTA
15	((Neisseria* NEAR1 mening*)) IN DARE, HTA
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
17	MeSH DESCRIPTOR Anti-Bacterial Agents EXPLODE ALL TREES IN DARE,HTA
18	MeSH DESCRIPTOR Penicillins EXPLODE ALL TREES IN DARE,HTA
19	MeSH DESCRIPTOR Cephalosporins EXPLODE ALL TREES IN DARE,HTA
20	MeSH DESCRIPTOR Cefotaxime EXPLODE ALL TREES IN DARE,HTA
21	MeSH DESCRIPTOR Amoxicillin EXPLODE ALL TREES IN DARE,HTA
22	MeSH DESCRIPTOR Ampicillin EXPLODE ALL TREES IN DARE,HTA
23	(((antibiotic* or antibacterial* or antibiotherap* or anti-biotic* or anti-bacterial* or anti-biotherap* or "anti biotic*" or "anti bacterial*" or "anti biotherap*"))) IN DARE, HTA
24	(((empiric* NEAR2 (therap* or treatment*)))) IN DARE, HTA
25	(((abbbocillin or adimicin or alcomicin or alpen or amblosin or amcill or amfipen or aminobenzylpenicillin or amox?cillin or amoxil* or ampicillin or ancef or anticepim or apogen or axepim* or ayercillin or benzo?penicillin* or benzyl?penicillin* or bicillin or binotal or biomox or bmy 28142 or bmy-28142 or bmy28142 or bristagen or bristamox or cedax or cefatriaxon* or cefepim* or cefixim* or cefizox or cefobid* or cefotan or cefotaxim* or ceftin or ceftriaxon* or ceftriazon* or cefuroxim* or cefzil or cepazin* or cephotaxim* or cephuroxim* or cepim?x or chloramphenicol or claforan or clamoxyl or compocillin or cosmopen or cotrimoxazol* or co trimoxazol* or co-trimoxazol or crysticillin or deripen or dexamethasone or diatracin or doktacillin or duricef or elobact or gelacillin or gentam?cin* or gent?mycin* or gentamyl* or gentamytrex or gentaplus or gentarad or gentaso* or gentasporin or gentatrim or gent?cin* or gent?cyn* or geocillin* or geomycin* or guicitrin* or hexam?cin* or hiconcil or histocillin or ibiamox or imacillin or jenamicin or kefurox or kefzol or klaforan or lendacin or longacef or longaceph or lyphocin or mandol or maxcef or maxipim* or mefoxin or megacillin or meropen* or miram?cin* or monocid or moxacin or oftagen* or omnipen or optigen* or penbritin* or penbrock or penicillin? or penicline or pentids or pentrex or pentrexl or pentrexyl or permapen or pfizerpen or polycillin or polymox or primafen or principen or refobacin* or ribom?cin* or rifampicin or rocefalin or rocefin or rocephin* or roscillin or sagestam* or spectrobid or sulm?cin* or supen or terram?cin* or totacillin or totapen or trimox or u?gencin* or ukapen or ultrabion or vamysin or vancam* or vanccostacin or vancin or vancom* or vancomycin or vankom* or velosef or vetramox* or viccillin or voncon* or wycillin or zimox or zinacef or zin?at))) IN DARE, HTA
26	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25
27	#16 AND #26

Economic Search

One global search was conducted for economic evidence across the guideline.

Database(s): NHS Economic Evaluation Database (NHS EED), HTA Database – CRD interface

Date of last search: 11 March 2021

#	Searches
1	MeSH DESCRIPTOR meningitis IN NHSEED,HTA
2	MeSH DESCRIPTOR Meningitis, Bacterial IN NHSEED,HTA
3	MeSH DESCRIPTOR Meningitis, Escherichia coli IN NHSEED,HTA
4	MeSH DESCRIPTOR Meningitis, Haemophilus EXPLODE ALL TREES IN NHSEED,HTA
5	MeSH DESCRIPTOR Meningitis, Listeria IN NHSEED,HTA
6	MeSH DESCRIPTOR Meningitis, Meningococcal IN NHSEED,HTA
7	MeSH DESCRIPTOR Meningitis, Pneumococcal IN NHSEED,HTA
8	MeSH DESCRIPTOR Meningoencephalitis IN NHSEED,HTA
9	(((bacter* or infect*) NEAR3 (meningit* or meninges* or leptomeninges* or subarachnoid space*))) IN NHSEED, HTA
10	((meningit* NEAR3 (e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon* or septic* or sepsis* or bacter?emi?))) IN NHSEED, HTA
11	(((e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or

#	Searches
	pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon*) NEAR3 (septic* or sepsis* or bacter?emi?))) IN NHSEED, HTA
12	((meningencephalitis* or meningoencephalitis* or meningit*)) IN NHSEED, HTA
13	MeSH DESCRIPTOR Meningococcal Infections IN NHSEED,HTA
14	MeSH DESCRIPTOR Neisseria meningitidis EXPLODE ALL TREES IN NHSEED,HTA
15	((meningococc* NEAR3 (sepsis* or septic* or toxic* or endotoxic* or disease* or infection*))) IN NHSEED, HTA
16	((meningococcus* or meningococci* or meningococcaemia* or meningococcemia*)) IN NHSEED, HTA
17	((Neisseria* NEXT mening*)) IN NHSEED, HTA
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 OR #16 OR #17

Database(s): Medline & Embase (Multifile) – OVID interface
Embase Classic+Embase 1947 to 2022 November 09, **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to November 09, 2022
Date of last search: 10 November 2022
Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	Meningitis/ or Meningitis, Bacterial/ or Meningitis, Escherichia Coli/ or Meningitis, Haemophilus/ or Meningitis, Listeria/ or Meningitis, Meningococcal/ or Meningitis, Pneumococcal/ or Meningoencephalitis/
2	1 use ppez
3	meningitis/ or bacterial meningitis/ or haemophilus meningitis/ or listeria meningitis/ or pneumococcal meningitis/ or meningoencephalitis/
4	3 use emczd
5	((bacter* or infect*) adj3 (meningit* or meninges* or leptomeninges* or subarachnoid space?)).ti,ab.
6	(meningit* adj3 (e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon* or septic* or sepsis* or bacter?emi?)).ti,ab.
7	((e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon*) adj3 (septic* or sepsis* or bacter?emi?)).ti,ab.
8	(mening?encephalitis* or meningit*).ti,ab.
9	or/2,4-8
10	Meningococcal Infections/ or exp Neisseria meningitidis/
11	10 use ppez
12	Meningococcosis/ or Meningococcemia/ or Neisseria Meningitidis/
13	12 use emczd
14	(meningococc* adj3 (sepsis* or septic* or toxic* or endotoxic* or disease? or infection?)).ti,ab.
15	(meningococcus* or meningococci* or meningococc?emi?).ti,ab.
16	(Neisseria* mening* or n mening*).ti,ab.
17	or/11,13-16
18	Economics/ use ppez
19	Value of life/ use ppez
20	exp "Costs and Cost Analysis"/ use ppez
21	exp Economics, Hospital/ use ppez
22	exp Economics, Medical/ use ppez
23	Economics, Nursing/ use ppez
24	Economics, Pharmaceutical/ use ppez
25	exp "Fees and Charges"/ use ppez
26	exp Budgets/ use ppez
27	health economics/ use emczd
28	exp economic evaluation/ use emczd
29	exp health care cost/ use emczd
30	exp fee/ use emczd
31	budget/ use emczd
32	funding/ use emczd
33	budget*.ti,ab.
34	cost*.ti.
35	(economic* or pharmaco?economic*).ti.
36	(price* or pricing*).ti,ab.
37	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38	(financ* or fee or fees).ti,ab.
39	(value adj2 (money or monetary)).ti,ab.
40	or/18-39
41	Quality-Adjusted Life Years/ use ppez
42	Sickness Impact Profile/
43	quality adjusted life year/ use emczd

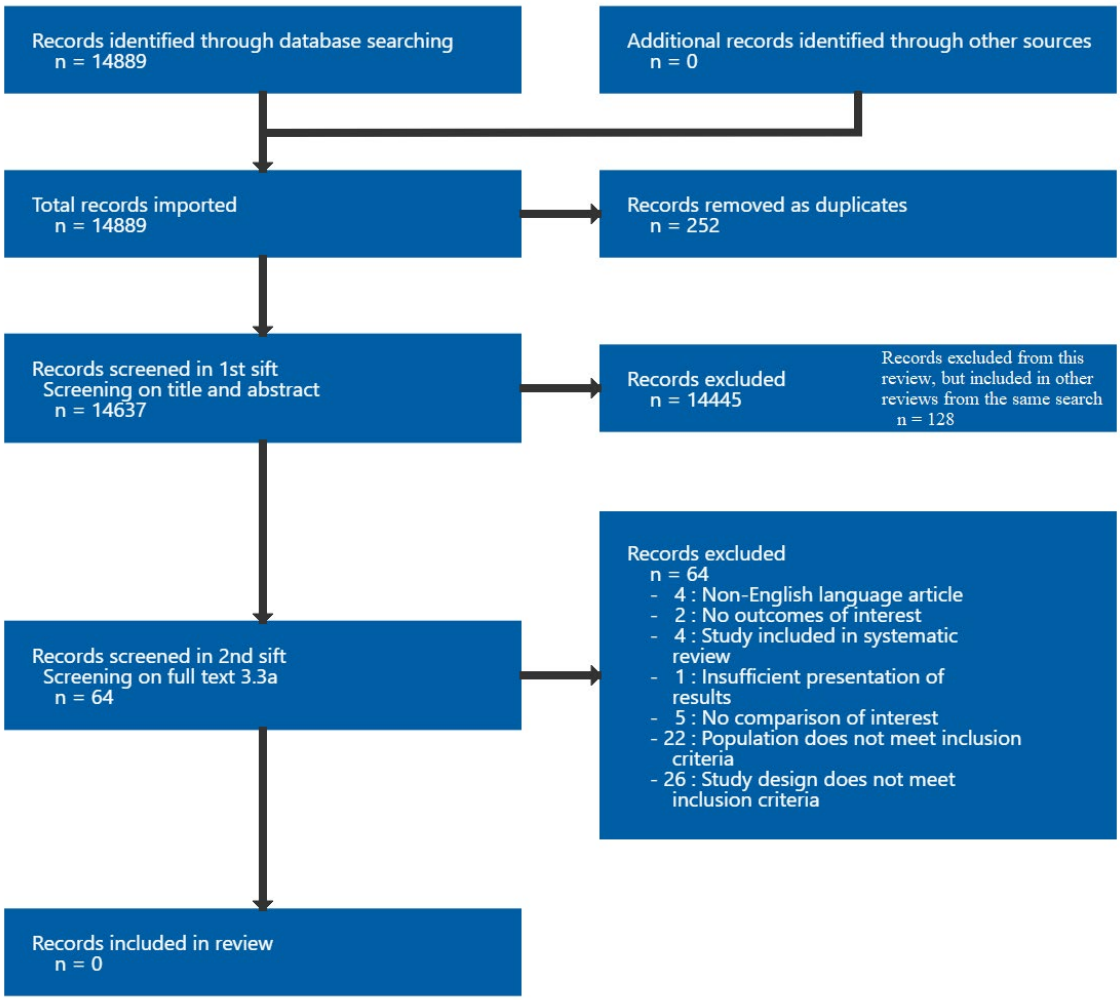
#	Searches
44	"quality of life index"/ use emczd
45	(quality adjusted or quality adjusted life year*).tw.
46	(qaly* or qal or qald* or qale* or qtime* or qwb* or daly).tw.
47	(illness state* or health state*).tw.
48	(hui or hui2 or hui3).tw.
49	(multiattibute* or multi attribute*).tw.
50	(utilit* adj3 (score*1 or valu* or health* or cost* or measur* or disease* or mean or gain or gains or index*)).tw.
51	utilities.tw.
52	(eq-5d* or eq5d* or eq-5* or eq5* or euroqual* or euro qual* or euroqual 5d* or euro qual 5d* or euro qol* or euroqol*or euro quol* or euroquol* or euro quol5d* or euroquol5d* or eur qol* or eurqol* or eur qol5d* or eurqol5d* or eur?qul* or eur?qul5d* or euro* quality of life or european qol).tw.
53	(euro* adj3 (5 d* or 5d* or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).tw.
54	(sf36 or sf 36 or sf thirty six or sf thirtysix).tw.
55	(time trade off*1 or time tradeoff*1 or tto or timetradeoff*1).tw.
56	Quality of Life/ and ((quality of life or qol) adj (score*1 or measure*1)).tw.
57	Quality of Life/ and ec.fs.
58	Quality of Life/ and (health adj3 status).tw.
59	(quality of life or qol).tw. and Cost-Benefit Analysis/ use ppez
60	(quality of life or qol).tw. and cost benefit analysis/ use emczd
61	((qol or hrqol or quality of life).tw. or *quality of life/) and ((qol or hrqol* or quality of life) adj2 (increas* or decreas* or improv* or declin* or reduc* or high* or low* or effect or effects or worse or score or scores or change*1 or impact*1 or impacted or deteriorat*)).ab.
62	Cost-Benefit Analysis/ use ppez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
63	cost benefit analysis/ use emczd and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
64	*quality of life/ and (quality of life or qol).ti.
65	quality of life/ and ((quality of life or qol) adj3 (improv* or chang*)).tw.
66	quality of life/ and health-related quality of life.tw.
67	Models, Economic/ use ppez
68	economic model/ use emczd
69	care-related quality of life.tw,kw.
70	((capability$ or capability-based$) adj (measure$ or index or instrument$)).tw,kw.
71	social care outcome$.tw,kw.
72	(social care and (utility or utilities)).tw,kw.
73	or/41-72
74	(9 or 17) and 40
75	(9 or 17) and 73
76	letter/
77	editorial/
78	news/
79	exp historical article/
80	Anecdotes as Topic/
81	comment/
82	case report/
83	(letter or comment*).ti.
84	76 or 77 or 78 or 79 or 80 or 81 or 82 or 83
85	randomized controlled trial/ or random*.ti,ab.
86	84 not 85
87	animals/ not humans/
88	exp Animals, Laboratory/
89	exp Animal Experimentation/
90	exp Models, Animal/
91	exp Rodentia/
92	(rat or rats or mouse or mice).ti.
93	86 or 87 or 88 or 89 or 90 or 91 or 92
94	letter.pt. or letter/
95	note.pt.
96	editorial.pt.
97	case report/ or case study/
98	(letter or comment*).ti.
99	94 or 95 or 96 or 97 or 98
100	randomized controlled trial/ or random*.ti,ab.
101	99 not 100
102	animal/ not human/
103	nonhuman/
104	exp Animal Experiment/
105	exp Experimental Animal/
106	animal model/
107	exp Rodent/
108	(rat or rats or mouse or mice).ti.

#	Searches
109	101 or 102 or 103 or 104 or 105 or 106 or 107 or 108
110	93 use ppez
111	109 use emczd
112	110 or 111
113	74 not 112
114	limit 113 to English language
115	75 not 112
116	limit 115 to English language
117	114 or 116

Appendix C Effectiveness evidence study selection

Study selection for: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

No evidence was identified which was applicable to this review question.

Appendix E Forest plots

Forest plots for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

No evidence was identified for this review question and so there are no forest plots.

Appendix F GRADE tables

GRADE tables for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

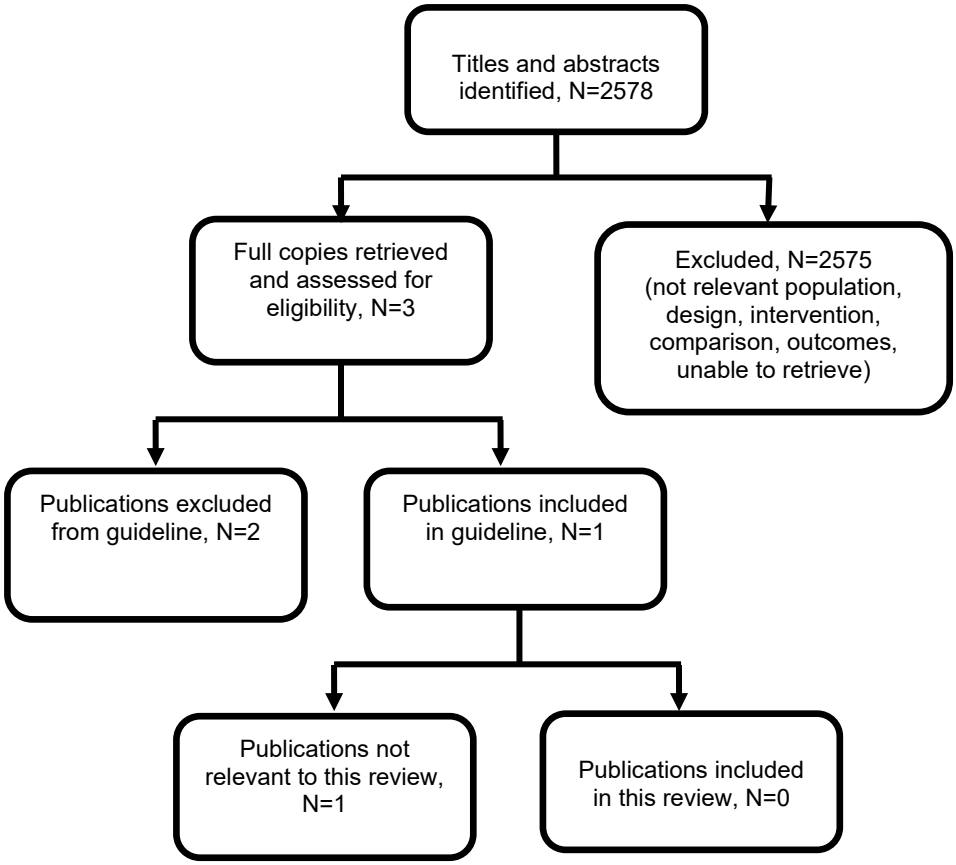
No evidence was identified which was applicable to this review question.

Appendix G Economic evidence study selection

Study selection for: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

A global economic search was undertaken for the whole guideline, but no economic evidence was identified which was applicable to this review question (see Figure 2).

Figure 2: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

No evidence was identified which was applicable to this review question.

Appendix I Economic model

Economic model for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

Excluded effectiveness studies

The excluded studies table only lists the studies that were considered and then excluded at the full-text stage for this review (N=64) and not studies (N=128) that were considered and then excluded from the search at the full-text stage as per the PRISMA diagram in Appendix C for the other review questions in the same search.

Table 3: Excluded studies and reasons for their exclusion

Study	Code [Reason]
(1993) Long-acting chloramphenicol for bacterial meningitis. Bulletin of the World Health Organization 71(1): 117-8, 123	- Study design does not meet inclusion criteria
Anonymous (1998) Antimicrobial therapy in the management of bacterial meningitis. WHO Drug Information 12(2): 70-72	- Study design does not meet inclusion criteria
Anonymous (1990) Ceftriaxone in the treatment of meningitis, gonococcal infections and other serious bacterial infections. Infectious Diseases and Immunization Committee, Canadian Paediatric Society. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 142(5): 450-2	- Study design does not meet inclusion criteria
Anonymous (1986) Initial antibiotic treatment of bacterial meningitis in children. Infectious Diseases and Immunization Committee, Canadian Paediatric Society. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 135(10): 1085-6	- Study design does not meet inclusion criteria
Anonymous (1997) Therapy for children with invasive pneumococcal infections. American Academy of Pediatrics Committee on Infectious Diseases. Pediatrics 99(2): 289-99	- Study design does not meet inclusion criteria
Anonymous (1995) Meropenem: A new carbapenem with potential for treating bacterial meningitis. Drugs and Therapy Perspectives 6(10): 1-5	- Study design does not meet inclusion criteria
Anonymous (1988) American Academy of Pediatrics Committee on Infectious Diseases: Treatment of bacterial meningitis. Pediatrics 81(6): 904-907	- Study design does not meet inclusion criteria
Anonymous (2010) Initiate appropriate	- Study design does not meet inclusion criteria

Study	Code [Reason]
antibacterial and adjunctive therapies when treating bacterial meningitis. Drugs and Therapy Perspectives 26(8): 19-22	
Anttila, M., Anttolainen, I., Ellmén, J. et al. (1991) (Antibiotics for bacterial meningitis in children - results of a Finnish multicentre trial). Duodecim; laaketieteellinen aikakauskirja 107: 149-157	- Non-English language article
Anttila, M., Anttolainen, I., Ellmén, J. et al. (1991) Antibiotic treatment of bacterial meningitis in children--results from a Finnish multicenter study. Duodecim; laaketieteellinen aikakauskirja 107(3): 149-157	- Non-English language article
Aronoff, S. C., Reed, M. D., O'Brien, C. A. et al. (1984) Comparison of the efficacy and safety of ceftriaxone to ampicillin/chloramphenicol in the treatment of childhood meningitis. Journal of antimicrobial chemotherapy 13(2): 143-151	- Study included in systematic review – Prasad 2007 (included in evidence review 3.3b)
Barson, W. J., Miller, M. A., Brady, M. T. et al. (1985) Prospective comparative trial of ceftriaxone vs. conventional therapy for treatment of bacterial meningitis in children. Pediatric infectious disease 4(4): 362-368	- Study included in systematic review – Prasad 2007(included in evidence review 3.3b)
Bass, J. W.; Person, D. A.; Fonseca, R. J. (1990) Cefuroxime versus ceftriaxone for bacterial meningitis (I). Journal of pediatrics 116(3): 488	- Study design does not meet inclusion criteria
Begue, P., Astruc, J., Francois, P. et al. (1998) Comparison of ceftriaxone and cefotaxime in severe pediatric bacterial infection: a multicentric study. Medecine ET maladies infectieuses 28(4): 300-306	- Non-English language article
Bijlsma, Merijn W., Brouwer, Matthijs C., Kasanmoentalib, E. Soemirien et al. (2016) Community-acquired bacterial meningitis in adults in the Netherlands, 2006-14: a prospective cohort study. The Lancet. Infectious diseases 16(3): 339-47	- Study design does not meet inclusion criteria
Bilal, Ali, Taha, Muhamed-Kheir, Caeymaex, Laurence et al. (2016) Neonatal Meningococcal Meningitis In France From 2001 To 2013. The Pediatric infectious disease journal 35(11): 1270-1272	- No comparison of interest for review
Bingen, Edouard, Levy, Corinne, de la Rocque, France et al. (2005) Bacterial meningitis in children: a French prospective study. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 41(7): 1059-63	- No comparison of interest for review
Bulloch, B.; Craig, W. R.; Klassen, T. P. (1997) The use of antibiotics to prevent serious sequelae	- Population does not meet inclusion criteria

Study	Code [Reason]
in children at risk for occult bacteremia: a meta-analysis. Academic Emergency Medicine 4(7): 679-683	
Cantey, Joseph B., Lopez-Medina, Eduardo, Nguyen, Sean et al. (2015) Empiric Antibiotics for Serious Bacterial Infection in Young Infants: Opportunities for Stewardship. Pediatric emergency care 31(8): 568-71	- Population does not meet inclusion criteria
Chaudhary, M.; Shrivastava, S. M.; Sehgal, R. (2008) Efficacy and safety study of fixed-dose combination of ceftriaxone-vancomycin injection in patients with various infections. Current drug safety 3(1): 82-85	- Population does not meet inclusion criteria
Chowdhary, G.; Dutta, S.; Narang, A. (2006) Randomized controlled trial of 7-Day vs. 14-Day antibiotics for neonatal sepsis. Journal of tropical pediatrics 52(6): 427-32	- Population does not meet inclusion criteria
Coon, Eric R., Srivastava, Raj, Stoddard, Greg et al. (2018) Shortened IV Antibiotic Course for Uncomplicated, Late-Onset Group B Streptococcal Bacteremia. Pediatrics 142(5)	- Population does not meet inclusion criteria
de Louvois, J.; Mulhall, A.; Hurley, R. (1982) Cefuroxime in the treatment of neonates. Archives of disease in childhood 57(1): 59-62	- No comparison of interest for review
del Rio, M. A., Chrane, D., Shelton, S. et al. (1983) Ceftriaxone versus ampicillin and chloramphenicol for treatment of bacterial meningitis in children. Lancet (london, england) 1(8336): 1241-1244	- Study included in systematic review – Prasad 2007 (included in evidence review 3.3b)
Donnelly, P. C., Sutich, R. M., Easton, R. et al. (2017) Ceftriaxone-Associated Biliary and Cardiopulmonary Adverse Events in Neonates: A Systematic Review of the Literature. Pediatric Drugs 19(1): 21-34	- Population does not meet inclusion criteria
Feldman, E. A., McCulloh, R. J., Myers, A. L. et al. (2017) Empiric antibiotic use and susceptibility in infants with bacterial infections: A multicenter retrospective cohort study. Hospital Pediatrics 7(8): 427-435	- No outcomes of interest for review
Furyk, J. S.; Swann, O.; Molyneux, E. (2011) Systematic review: neonatal meningitis in the developing world. Tropical medicine & international health : TM & IH 16(6): 672-9	- No comparison of interest for review
Haffejee, I. E. (1984) A therapeutic trial of cefotaxime versus penicillin-gentamicin for severe infections in children. Journal of antimicrobial chemotherapy 14supplb: 147-152	- Population does not meet inclusion criteria
Haffejee, I. E. (1988) Cefotaxime versus	- Study included in systematic review – Prasad

Study	Code [Reason]
penicillin-chloramphenicol in purulent meningitis: a controlled single-blind clinical trial. Annals of tropical paediatrics 8(4): 225-9	2007 (included in evidence review 3.3b)
Hodgson, Kate Alison, Lim, Ruth, Huynh, Julie et al. (2022) Outpatient parenteral antimicrobial therapy: how young is too young?. Archives of disease in childhood	- Study design does not meet inclusion criteria
Johansson, O.; Cronberg, S.; Hoffstedt, B. (1982) Cefuroxime versus ampicillin and chloramphenicol for the treatment of bacterial meningitis. Report from a Swedish study group. Lancet 1(8267): 295-299	- Population does not meet inclusion criteria
Joubrel, C., Tazi, A., Six, A. et al. (2015) Group B streptococcus neonatal invasive infections, France 2007-2012. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 21(10): 910-6	- Study design does not meet inclusion criteria
Karageorgopoulos, D. E., Valkimadi, P. E., Kapaskelis, A. et al. (2009) Short versus long duration of antibiotic therapy for bacterial meningitis: a meta-analysis of randomised controlled trials in children. Archives of Disease in Childhood 94(8): 607-614	- Population does not meet inclusion criteria
Kasiakou, S. K., Sermaides, G. J., Michalopoulos, A. et al. (2005) Continuous versus intermittent intravenous administration of antibiotics: A meta-analysis of randomised controlled trials. Lancet Infectious Diseases 5(9): 581-589	- Population does not meet inclusion criteria
Kecmanovic, M.; Pavlovic, M.; Kostic, A. (1982) Cefotaxime in the treatment of suppurative meningitis. Chemioterapia 1(4suppl): 85	- Study design does not meet inclusion criteria
Klugman, K. P. and Dagan, R. (1995) Randomized comparison of meropenem with cefotaxime for treatment of bacterial meningitis. Meropenem Meningitis Study Group. Antimicrobial agents and chemotherapy 39(5): 1140-1146	- Population does not meet inclusion criteria
Korbila, I. P., Tansarli, G. S., Karageorgopoulos, D. E. et al. (2013) Extended or continuous versus short-term intravenous infusion of cephalosporins: A meta-analysis. Expert Review of Anti-Infective Therapy 11(6): 585-595	- Population does not meet inclusion criteria
Levine, D. P.; McNeil, P.; Lerner, S. A. (1989) Randomized, double-blind comparative study of intravenous ciprofloxacin versus ceftazidime in the treatment of serious infections. American journal of medicine 87(5a): 160S-163S	- Population does not meet inclusion criteria
Madson, L. and Grose, C. (1990) Ceftriaxone vs	- Study design does not meet inclusion criteria

Study	Code [Reason]
cefotaxime for treatment of Haemophilus influenzae meningitis (I). Pediatrics 85(4): 622-623	
Marget, W.; Belohradsky, B. H.; Roos, R. (1980) Guidelines for adequate chemotherapeutic dosage in newborns and infants with septicaemia and meningitis. Infection suppl1: 82-6	- Study design does not meet inclusion criteria
Martin, E., Hohl, P., Guggi, T. et al. (1990) Short course single daily ceftriaxone monotherapy for acute bacterial meningitis in children: results of a Swiss multicenter study. Part I: clinical results. Infection 18(2): 70-77	- Population does not meet inclusion criteria
Mathur, N. B.; Kharod, P.; Kumar, S. (2015) Evaluation of duration of antibiotic therapy in neonatal bacterial meningitis: a randomized controlled trial. Journal of tropical pediatrics 61(2): 119-125	- Population does not meet inclusion criteria
McCracken Jr, G. H. (1986) Aminoglycoside toxicity in infants and children. American Journal of Medicine 80(6b): 172-178	- Study design does not meet inclusion criteria
McGee, Lesley, Chochua, Sopio, Li, Zhongya et al. (2020) Multistate, population-based distributions of candidate vaccine targets, clonal complexes, and resistance features of invasive Group B Streptococci within the US: 2015-2017. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America	- No comparison of interest for review
McGill, F., Heyderman, R. S., Michael, B. D. et al. (2016) The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. The Journal of infection 72(4): 405-38	- Study design does not meet inclusion criteria
Molyneux, E. M., Dube, Q., Banda, F. M. et al. (2017) The Treatment of Possible Severe Infection in Infants: an Open Randomized Safety Trial of Parenteral Benzylpenicillin and Gentamicin Versus Ceftriaxone in Infants <60 days of Age in Malawi. Pediatric infectious disease journal 36(12): e328-e333	- Population does not meet inclusion criteria
O'Neill, P. (1993) How long to treat bacterial meningitis. Lancet (London, England) 341(8844): 530	- Study design does not meet inclusion criteria
Okike, I. O., Awofisayo, A., Adak, B. et al. (2015) Empirical antibiotic cover for Listeria monocytogenes infection beyond the neonatal period: A time for change?. Archives of Disease in Childhood 100(5): 423-425	- Study design does not meet inclusion criteria
Onakpoya, Igho J., Walker, A. Sarah, Tan, Pui S.	- Insufficient presentation of results

Study	Code [Reason]
et al. (2018) Overview of systematic reviews assessing the evidence for shorter versus longer duration antibiotic treatment for bacterial infections in secondary care. PloS one 13(3): e0194858	
Pintado, Vicente, Cabellos, Carmen, Moreno, Santiago et al. (2003) Enterococcal meningitis: a clinical study of 39 cases and review of the literature. Medicine 82(5): 346-64	- Study design does not meet inclusion criteria
Romain, O. (2017) Antibiotherapy for early-onset neonatal bacterial infections in newborn borns > 34 week's gestation. Archives de Pediatrie 24(supplement3): S24-S28	- Non-English language article
Schaad, U. B. (1984) The cephalosporin compounds in severe neonatal infection. European journal of pediatrics 141(3): 143-6	- Study design does not meet inclusion criteria
Schaad, U. B., Suter, S., Gianella-Borradori, A. et al. (1990) A comparison of ceftriaxone and cefuroxime for the treatment of bacterial meningitis in children. New England journal of medicine 322(3): 141-147	- Population does not meet inclusion criteria
Scholz, H., Hofmann, T., Noack, R. et al. (1998) Prospective comparison of ceftriaxone and cefotaxime for the short-term treatment of bacterial meningitis in children. Chemotherapy 44(2): 142-147	- Population does not meet inclusion criteria
Steele, R. W.; Steele, A. J.; Gelzine, A. L. (1992) Ceftriaxone and bacterial meningitis. A ten-year follow-up. Antibiotics and chemotherapy 45: 161-168	- Study design does not meet inclusion criteria
Tetanye, E., Yondo, D., Bernard-Bonnin, A. C. et al. (1990) Initial treatment of bacterial meningitis in Yaounde, Cameroon: theoretical benefits of the ampicillin-chloramphenicol combination versus chloramphenicol alone. Annals of tropical paediatrics 10(3): 285-291	- Population does not meet inclusion criteria
Tunkel, Allan R. (2006) Use of ceftriaxone during epidemics in patients with suspected meningococcal meningitis. Current infectious disease reports 8(4): 291-2	- Population does not meet inclusion criteria
van de Beek, D., Cabellos, C., Dzupova, O. et al. (2016) ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 22suppl3: S37-62	- Study design does not meet inclusion criteria
Van Reempts, P. J., Van Overmeire, B., Mahieu, L. M. et al. (1995) Clinical experience with ceftriaxone treatment in the neonate.	- Population does not meet inclusion criteria

Study	Code [Reason]
Chemotherapy 41(4): 316-22	
Watanakunakorn, C., Greifenstein, A., Stroh, K. et al. (1993) Pneumococcal bacteremia in three community teaching hospitals from 1980 to 1989. Chest 103(4): 1152-6	- Population does not meet inclusion criteria
Weiss, D. and Glaser, J. H. (1990) Ceftriaxone versus cefuroxime for treatment of bacterial meningitis. Journal of pediatrics 116(3): 492	- Study design does not meet inclusion criteria
Wintenberger, C., Guery, B., Bonnet, E. et al. (2017) Proposal for shorter antibiotic therapies. Medecine et maladies infectieuses 47(2): 92-141	- Study design does not meet inclusion criteria
Woods, C. R. (2018) Uncomplicated late-onset group b streptococcal bacteremia: Can we do less than 10 days IV?. Pediatrics 142(5): e20182623	- Study design does not meet inclusion criteria
Zhao, Zhi, Hua, Xueying, Yu, Jialin et al. (2019) Duration of empirical therapy in neonatal bacterial meningitis with third generation cephalosporin: a multicenter retrospective study. Archives of medical science : AMS 15(6): 1482-1489	- Population does not meet inclusion criteria

Excluded economic studies

No studies were identified which were applicable to this review question.

Appendix K Research recommendations – full details

Research recommendations for review question: What antibiotic treatment regimens are effective in treating suspected bacterial meningitis in younger infants before identifying the causative infecting organism, or in the absence of identifying the causative infecting organism?

No research recommendation was made for this review.