

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

**[E3] Evidence review for antibiotics for bacterial meningitis caused by Group B streptococcus**

*NICE guideline number tbc*

*Evidence review underpinning recommendations 1.6.4, 1.6.12 and 1.6.16 in the NICE guideline*

*September 2023*

*Draft for consultation*

*This evidence review was developed by NICE*



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# 1 Antibiotics for bacterial meningitis caused 2 by Group B streptococcus

## 3 Review question

4 What antibiotic treatment regimens are effective in treating bacterial meningitis caused by  
5 Group B streptococcus?

## 6 Introduction

7 Bacterial meningitis is a rare but serious infection. The causative organism is usually  
8 confirmed by tests performed on cerebrospinal fluid or blood samples. Group B  
9 streptococcus is a common cause of bacterial meningitis in neonates and younger babies,  
10 and more rarely in adults.

11 The aim of this review is to determine what antibiotic treatment regimens are effective in  
12 treating bacterial meningitis caused by Group B streptococcus.

## 13 Summary of the protocol

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

16 **Table 1: Summary of the protocol (PICO table)**

<b>Population</b>	All adults, young people, children and babies (excluding neonates defined as aged 28 days old and younger) with confirmed bacterial meningitis caused by Group B streptococcus
<b>Intervention</b>	Antibiotic agent of interest: <ul style="list-style-type: none"><li>• Ampicillin</li><li>• Amoxicillin</li><li>• Benzylpenicillin sodium</li><li>• Cefotaxime</li><li>• Ceftriaxone</li><li>• Gentamicin</li><li>• Meropenem</li></ul> Beta-lactam allergy: <ul style="list-style-type: none"><li>• Chloramphenicol (adults only)</li></ul>
<b>Comparison</b>	<b>Stage 1 (all antibiotic agents of interest):</b> <ul style="list-style-type: none"><li>• Antibiotic agent A (single or combination)* vs Antibiotic agent B (single or combination)*</li></ul> *Gentamycin to be used in combination with other antibiotics not monotherapy. <b>Stage 2 (antibiotic agents identified during stage 1 as most effective/for use where there are contraindications)</b> Comparisons: <ul style="list-style-type: none"><li>• Antibiotic agent A – Dose A vs Antibiotic agent A – Dose B</li><li>• Antibiotic agent A – Duration of administration A vs Antibiotic agent A – Duration of administration B</li><li>• Antibiotic agent A – Short infusion vs Antibiotic agent A – Extended infusion</li></ul>
<b>Outcome</b>	<b>Critical</b> Population: adults, children and infants <ul style="list-style-type: none"><li>• All-cause mortality (measured up to 1 year after discharge)</li></ul>

- 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)

Population: adults

- Functional impairment (measured by any validated scale at any time point)

Population: children and infants

- 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

Population: adults, children and infants

- Hearing impairment (defined as any level of hearing impairment; measured from discharge up to 1 year after discharge)
- Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant
- CSF sterilisation (defined as treatment failure, time-to-sterilisation or delay)

Population: adults

- Intracranial collections as a complication (defined as abscess or empyema)

Population: children and infants

- Functional impairment (measured by any validated scale at any time point)

\*For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age.

1 CSF: cerebrospinal fluid; MDI: mental development index; PDI: psychomotor development index; SD: standard  
2 deviation

3 For further details see the review protocol in appendix A.

## 4 **Methods and process**

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

9 Declarations of interest were recorded according to [NICE's conflicts of interest policy](#).

## 10 **Effectiveness evidence**

### 11 **Included studies**

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

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

### 15 **Excluded studies**

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

## 1 **Summary of included studies**

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

## 5 **Summary of the evidence**

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

## 8 **Economic evidence**

### 9 **Included studies**

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

### 13 **Economic model**

14 No economic modelling was undertaken for this review because the committee agreed that  
15 other topics were higher priorities for economic evaluation.

## 16 **The committee's discussion and interpretation of the evidence**

### 17 **The outcomes that matter most**

18 Bacterial meningitis is associated with high rates of mortality and morbidity, and antibiotics  
19 are the mainstay of treatment for bacterial meningitis. Therefore, all-cause mortality and  
20 long-term neurological impairment were prioritised as critical outcomes due to the severity of  
21 these outcomes. Severe developmental delay was prioritised over functional impairment in  
22 children and babies, as it is a more relevant and important outcome for this population.  
23 Functional impairment was prioritised as a critical outcome in adults due to the concern  
24 about the potential long-term limitations of bacterial meningitis on the ability to carry out  
25 certain activities of daily life.

26 In addition to functional impairment (in children and babies), hearing impairment, serious  
27 intervention-related adverse effects, and cerebrospinal fluid (CSF) sterilisation were selected  
28 as important outcomes in all age groups as these are relatively common after bacterial  
29 meningitis and may be related to antibiotic therapy. Intracranial collections as a complication  
30 was also included as an important outcome for adults as this is a rare but severe and life  
31 threatening complication of bacterial meningitis that may require prolonged antibiotic  
32 treatment.

### 33 **The quality of the evidence**

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

### 35 **Benefits and harms**

36 No evidence was identified on the effectiveness of antibiotics for the treatment of group B  
37 streptococcal meningitis. Based on their clinical knowledge and experience, and on current  
38 practice, the committee recommended ceftriaxone in line with the BNF (Joint Formulary  
39 Committee 2022) and BNFC (Paediatric Formulary Committee 2022), for the treatment of  
40 group B streptococcal meningitis.



1 The committee were aware that the previous NICE guideline on meningitis (NICE 2010)  
2 recommended that group B streptococcal meningitis is treated with cefotaxime. However, the  
3 committee highlighted the potential practical and resource-use advantages associated with  
4 ceftriaxone because the long half-life means that it can be given only once a day. The  
5 committee acknowledged some concerns with once daily administration in that a second  
6 dose might need to be delayed if the first dose of ceftriaxone was administered outside of  
7 routine working hours; however, they were aware that a second dose can be given earlier, to  
8 shift the administration time, if there is a minimum of 12 hours between doses (Gbesemete  
9 2019).

10 The committee discussed some reasons why in clinical practice (particularly in intensive care  
11 units) cefotaxime might be given instead of ceftriaxone. For instance, to minimise the time  
12 that intravenous lines are being used for administering antibiotics, which might be needed for  
13 other medications, due to ceftriaxone typically being infused over 30 minutes intravenous  
14 and cefotaxime being given as a bolus. However, the committee agreed that this practice is  
15 not necessary, as ceftriaxone can be given as bolus. Sometimes there may be a reaction (for  
16 example, vomit reflex) if ceftriaxone is administered too quickly, but in the committee's  
17 experience this is relatively rare, which was supported by a recent study (Patel 2021). The  
18 committee agreed that ceftriaxone should be given as first-line treatment for group B  
19 streptococcal meningitis, unless contraindicated in which case cefotaxime can be  
20 considered. The committee highlighted contraindications around pre-term babies less than  
21 41 weeks corrected gestational age and included a reference to these in the BNFC in the  
22 recommendation in order to raise awareness.

23 The committee recognised that the clinical course of group B streptococcal meningitis can be  
24 complicated, particularly in young babies where Group B streptococcus is an important  
25 cause (relative to adults where this is rare). Based on their clinical knowledge and  
26 experience, the committee recommended that advice is sought from an infection specialist (a  
27 microbiologist or infectious diseases specialist) for the treatment of group B streptococcal  
28 meningitis.

29 The committee recommended that antibiotic treatment should continue for at least 14 days.  
30 This is in line with the cephalosporin treatment duration recommended in the previous NICE  
31 guideline on bacterial meningitis (NICE 2010). The committee acknowledged that treatment  
32 could continue up to 21 days, but agreed to specify a minimum duration and any further  
33 extension of treatment duration could be considered with advice from an infection specialist  
34 and depending on the specific individualised characteristics of the person with group B  
35 streptococcal meningitis.

36 There was no evidence found on antibiotic use for group B streptococcal meningitis in people  
37 with a penicillin allergy, but the committee agreed it was important to make a  
38 recommendation for this population. Based on their clinical knowledge and experience, the  
39 committee agreed that cephalosporin-induced anaphylaxis is rare, and the risk-benefit  
40 balance of a cephalosporin (relative to chloramphenicol as an alternative) is favourable in  
41 most patients with non-anaphylactic penicillin allergy. Therefore, the committee agreed that  
42 clinicians should seek information about the nature of the allergy and advice from an  
43 infection specialist before making a treatment decision. The committee acknowledged that it  
44 is important that treatment is not delayed; however, they agreed that information about the  
45 nature of allergy is often readily available from the patient's family. The committee agreed  
46 that a cephalosporin should still be considered if the nature of the allergic reaction they get is  
47 non-anaphylactic or non-severe, in accordance with the first line treatment recommended  
48 above. However, if the allergic reaction is anaphylactic or severe, alternatives to ceftriaxone  
49 or cefotaxime will be needed. The committee discussed that chloramphenicol is commonly  
50 used in the case of severe beta-lactam (penicillin, amoxicillin, or cephalosporin) allergy.  
51 Based on clinical knowledge and experience, the committee recommended chloramphenicol  
52 for people with group B streptococcal meningitis and anaphylactic or severe penicillin allergy.

1 The committee were aware that the previous NICE guideline on bacterial meningitis (NICE  
2 2010) recommended to treat people who have travelled outside the UK with vancomycin (in  
3 addition to the cephalosporin). However, they discussed that practice has changed since the  
4 previous NICE guideline. The committee were aware that current practice is to use rifampicin  
5 or linezolid in addition to a cephalosporin where the cephalosporin itself might be insufficient  
6 due to resistance. However, the committee highlighted that there is not enough evidence to  
7 support recommending them. Therefore, the committee recommended that, clinicians should  
8 seek advice from an infection specialist if cephalosporin resistance is suspected in people  
9 who have recently travelled abroad.

10 Given that no evidence was identified for this review the committee discussed including a  
11 research recommendation on the effectiveness of antibiotics for the treatment of group B  
12 streptococcal meningitis. However, the committee agreed that given this condition is rare it  
13 would be unlikely that a clinical trial would be feasible.

#### 14 **Cost effectiveness and resource use**

15 This review question was not prioritised for economic analysis and therefore the committee  
16 made a qualitative assessment of the likely cost-effectiveness of their recommendations. The  
17 committee considered that in the absence of evidence it would be cost-effective to  
18 recommend ceftriaxone instead of cefotaxime. This is because ceftriaxone can be  
19 administered once daily making it more practical and less resource intensive. The committee  
20 believed that this change from previous NICE guidance (NICE 2010) could result in some  
21 small cost savings for the NHS.

#### 22 **Recommendations supported by this evidence review**

23 This evidence review supports recommendations 1.6.4, 1.6.12 and 1.6.16. Other evidence  
24 supporting the recommendations 1.6.4 and 1.6.16 can be found in evidence reviews on  
25 antibiotic regimens for bacterial meningitis before or in the absence of identifying causative  
26 infecting organism (see evidence reviews D1 to D3) and for specific causative organisms  
27 (see evidence reviews E1, E2 and E4 to E6).  
28

1

## 2 **References – included studies**

### 3 **Effectiveness**

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

### 5 **Economic**

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

### 7 **Other**

#### 8 **Gbesemete 2019**

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

#### 12 **Joint Formulary Committee 2022**

13 Joint Formulary Committee, British National Formulary (online). London: BMJ Group and  
14 Pharmaceutical Press. Available at: <http://www.medicinescomplete.com> [Accessed  
15 04/04/2022]

#### 16 **NICE 2010**

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

#### 20 **Paediatric Formulary Committee 2022**

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

#### 24 **Patel 2021**

25 Patel, S., Green. H., Gray, J., Rutter, M., Bevan, A., Hand, K., Jones, C. E., Faust, S. N.  
26 (2021). Evaluating Ceftriaxone 80 mg/kg Administration by Rapid Intravenous Infusion—A  
27 Clinical Service Evaluation. The Pediatric Infectious Disease Journal, 40(2), 128-129

28

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30

# 1 Appendices

## 2 Appendix A Review protocols

### 3 Review protocol for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis 4 caused by Group B streptococcus?

5 **Table 2: Review protocol**

Field	Content
PROSPERO registration number	CRD42021276573
Review title	Antibiotics for bacterial meningitis caused by Group B streptococcus
Review question	What antibiotic treatment regimens are effective in treating bacterial meningitis caused by Group B streptococcus?
Objective	This review aims to find out what is the optimal antibiotic treatment regimen in improving outcomes for people with bacterial meningitis caused by Group B streptococcus
Searches	<p>The following databases will be searched:</p> <ul style="list-style-type: none"><li>• Cochrane Central Register of Controlled Trials (CENTRAL)</li><li>• Cochrane Database of Systematic Reviews (CDSR)</li><li>• Embase</li><li>• MEDLINE</li></ul> <p>Searches will be restricted by:</p> <ul style="list-style-type: none"><li>• Date limitations: 1980</li><li>• English language</li><li>• Human studies</li></ul> <p>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.</p>

Field	Content
Condition or domain being studied	Bacterial meningitis caused by Group B streptococcus
Population	<p>Inclusion: All adults, young people, children and babies (excluding neonates defined as aged 28 days old and younger) with confirmed bacterial meningitis caused by Group B streptococcus</p> <p>Exclusion:</p> <p>People:</p> <ul style="list-style-type: none"> <li>• with known immunodeficiency.</li> <li>• 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.</li> <li>• with confirmed viral meningitis or viral encephalitis.</li> <li>• with confirmed tuberculous meningitis.</li> <li>• with confirmed fungal meningitis.</li> </ul>
Intervention/Exposure/Test	<p>Antibiotic agent of interest:</p> <ul style="list-style-type: none"> <li>• Ampicillin</li> <li>• Amoxicillin</li> <li>• Benzylpenicillin sodium</li> <li>• Cefotaxime</li> <li>• Ceftriaxone</li> <li>• Gentamicin</li> <li>• Meropenem</li> </ul> <p>Beta-lactam allergy:</p> <ul style="list-style-type: none"> <li>• Chloramphenicol (adults only)</li> </ul>
Comparator/Reference standard/Confounding factors	<p><b>Stage 1 (all antibiotic agents of interest):</b></p> <ul style="list-style-type: none"> <li>• Antibiotic agent A (single or combination)* vs Antibiotic agent B (single or combination)*</li> </ul>

Field	Content
	<p>*Gentamycin to be used in combination with other antibiotics not monotherapy.</p> <p><b>Stage 2 (antibiotic agents identified during stage 1 as most effective/for use where there are contraindications)</b></p> <p>Comparisons:</p> <ol style="list-style-type: none"> <li>1. Antibiotic agent A – Dose A vs Antibiotic agent A – Dose B</li> <li>2. Antibiotic agent A – Duration of administration A vs Antibiotic agent A – Duration of administration B</li> <li>3. Antibiotic agent A – Short infusion vs Antibiotic agent A – Extended infusion</li> </ol>
Types of study to be included	<p>Include published full-text papers:</p> <ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs</li> <li>• If insufficient RCTs: prospective cohort studies</li> <li>• If insufficient prospective cohort studies: retrospective cohort studies</li> </ul> <p>Non-randomised studies will be downgraded for risk of bias if they do not adequately adjust for the following covariates, but will not be excluded for this reason:</p> <ul style="list-style-type: none"> <li>• Co-morbidity</li> <li>• Severity of infection at presentation (including sepsis)</li> </ul> <p>Exclude:</p> <ul style="list-style-type: none"> <li>• Conference abstracts</li> </ul>
Other exclusion criteria	<ul style="list-style-type: none"> <li>• Cohort studies from low income countries.</li> <li>• Studies conducted prior to 1980 as currently used antibiotics were not in common usage prior to this date.</li> <li>• Studies published not in English-language</li> </ul>
Context	<p>This guidance will fully update the following: Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (CG102)</p>

Field	Content
Primary outcomes (critical outcomes)	<p><b>Adults</b></p> <ul style="list-style-type: none"> <li>All-cause mortality (measured up to 1 year after discharge)</li> <li>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)</li> <li>Functional impairment (measured by any validated scale at any time point)</li> </ul> <p><b>Children and infants</b></p> <ul style="list-style-type: none"> <li>All-cause mortality (measured up to 1 year after discharge)</li> <li>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)</li> <li>Severe developmental delay (defined as score of &gt;2 SD below normal on validated assessment scales, or MDI or PDI &lt;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)</li> </ul> <p>*For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age.</p>
Secondary outcomes (important outcomes)	<p><b>Adults</b></p> <ul style="list-style-type: none"> <li>Hearing impairment (defined as any level of hearing impairment; measured from discharge up to 1 year after discharge)</li> <li>Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant</li> <li>CSF sterilisation (defined as treatment failure, time-to-sterilisation or delay).</li> <li>Intracranial collections as a complication (defined as abscess or empyema)</li> </ul>

Field	Content
	<p><b>Children and infants</b></p> <ul style="list-style-type: none"> <li>• Hearing impairment (defined as any level of hearing impairment; measured from discharge up to 1 year after discharge)</li> <li>• Functional impairment (measured by any validated scale at any time point)</li> <li>• Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant</li> <li>• CSF sterilisation (defined as treatment failure, time to sterilisation or delay)</li> </ul>
Data extraction (selection and coding)	<p>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.</p>
Risk of bias (quality) assessment	<p>Quality assessment of individual studies will be performed using the following checklists:</p> <ul style="list-style-type: none"> <li>• ROBIS tool for systematic reviews</li> <li>• Cochrane RoB tool v.2 for RCTs and quasi-RCTs</li> <li>• Cochrane ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies</li> </ul> <p>The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.</p>
Strategy for data synthesis	<p>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</p>



Field	Content
	<p>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 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 <math>I^2</math> statistic. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through sensitivity 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: <a href="http://www.gradeworkinggroup.org/">http://www.gradeworkinggroup.org/</a></p> <p><b>Minimally important differences:</b></p> <ul style="list-style-type: none"> <li>• All-cause mortality: statistical significance</li> <li>• Serious intervention-related adverse effects: statistical significance</li> <li>• CSF sterilization: statistical significance</li> <li>• Intracranial collections: statistical significance</li> <li>• Validated scales: Published MIDs where available; if not GRADE default MIDs</li> <li>• All other outcomes: GRADE default MIDs</li> </ul>
Analysis of sub-groups	<p>Evidence will be stratified by:</p> <p><b>Stage 1</b></p> <ul style="list-style-type: none"> <li>• Age: <ul style="list-style-type: none"> <li>○ Younger Infants, older infants and children: &gt;28 days to &lt;18* years of age</li> <li>○ Adults: ≥18* years of age</li> </ul> </li> </ul> <p><b>Stage 2</b></p> <ul style="list-style-type: none"> <li>• Age:</li> </ul>

Field	Content														
	<ul style="list-style-type: none"> <li>○ Younger Infants: &gt;28 days to ≤3 months of age</li> <li>○ Older infants and children: &gt;3 months to &lt;18* years of age</li> <li>○ Adults: ≥18* years of age</li> </ul> <p>*There is variation in clinical practice regarding the treatment of 16 to 18 year olds. Therefore, we will be guided by cut-offs used in the evidence when determining if 16 to 18 year olds should be treated as adults or children.</p> <p>Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes:</p> <ul style="list-style-type: none"> <li>• Age:             <ul style="list-style-type: none"> <li>○ Young and middle aged adults</li> <li>○ Older adults*</li> </ul> </li> </ul> <p>*There is variation regarding the age at which adults should be considered older adults. Therefore, we will be guided by cut-offs used in the evidence when determining this threshold.</p> <p>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 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.</p>														
Type and method of review	<table border="1"> <tr> <td><input checked="" type="checkbox"/></td> <td>Intervention</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Diagnostic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Prognostic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Qualitative</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Epidemiologic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Service Delivery</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Other (please specify)</td> </tr> </table>	<input checked="" type="checkbox"/>	Intervention	<input type="checkbox"/>	Diagnostic	<input type="checkbox"/>	Prognostic	<input type="checkbox"/>	Qualitative	<input type="checkbox"/>	Epidemiologic	<input type="checkbox"/>	Service Delivery	<input type="checkbox"/>	Other (please specify)
<input checked="" type="checkbox"/>	Intervention														
<input type="checkbox"/>	Diagnostic														
<input type="checkbox"/>	Prognostic														
<input type="checkbox"/>	Qualitative														
<input type="checkbox"/>	Epidemiologic														
<input type="checkbox"/>	Service Delivery														
<input type="checkbox"/>	Other (please specify)														

Field	Content		
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	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Piloting of the study selection process	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Formal screening of search results against eligibility criteria	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Data extraction	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Risk of bias (quality) assessment	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Data analysis	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Named contact	Named contact: National Guideline Alliance		
	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		

Field	Content
	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 <a href="#">Developing NICE guidelines: the manual</a> . Members of the guideline committee are available on the NICE website: <a href="https://www.nice.org.uk/guidance/indevelopment/gid-ng10149">https://www.nice.org.uk/guidance/indevelopment/gid-ng10149</a> .
Other registration details	None
Reference/URL for published protocol	<a href="https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021276573">https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021276573</a>
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: <ul style="list-style-type: none"> <li>• notifying registered stakeholders of publication</li> <li>• publicising the guideline through NICE's newsletter and alerts</li> <li>• 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.</li> </ul>
Keywords	Bacterial meningitis, antibiotic, anti-bacterial, mortality, impairments
Details of existing review of same topic by same authors	None
Current review status	<input type="checkbox"/> Ongoing <input checked="" type="checkbox"/> Completed but not published <input type="checkbox"/> Completed and published <input type="checkbox"/> Completed, published and being updated <input type="checkbox"/> Discontinued
Additional information	None
Details of final publication	<a href="http://www.nice.org.uk">www.nice.org.uk</a>

1 CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CSF: cerebrospinal fluid; GRADE: Grading of  
2 Recommendations Assessment, Development and Evaluation; MDI: mental development index; MEDLINE: Medical Literature Analysis and Retrieval System Online; MID:

- 1 *minimally important difference; NICE: National Institute for Health and Care Excellence; PDI: psychomotor development index; PRESS: Peer Review of Electronic Search*
- 2 *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;*
- 3 *SD: standard deviation*

## 1 Appendix B Literature search strategies

### 2 Literature search strategies for review question: What antibiotic treatment 3 regimens are effective in treating bacterial meningitis caused by *Group B* 4 *streptococcus*?

5  
6 This was a combined search to cover both this review and D1, D2, D3, E1, E2, E4, E5, E6  
7 and F1 on antibiotic regimens for bacterial meningitis (before or in the absence of identifying  
8 causative infecting organism and for specific causative organisms) and meningococcal  
9 disease.

#### 10 11 12 Clinical Search

13  
14 Database(s): Medline & Embase (Multifile) – OVID interface  
15 Embase Classic+Embase 1947 to 2022 November 09, Ovid MEDLINE(R) and Epub  
16 Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to November  
17 09, 2022

18 Date of last search: 10 November 2022

19 Multifile database codes: emczd = Embase Classic+Embase; ppez = MEDLINE(R) and Epub Ahead of  
20 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 influenza* or h influenza* 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 influenza* or h influenza* 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	(abocillin 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 ceftriaxon* or cefepim* or cefixim* or cefizox or cefobid* or cefotan or cefotaxim* or ceftaroline* or ceftin or ceftolozane* or ceftriaxon* or ceftriaxon* or cefuroxim* or cezil or cepazin* or cephalosporin* or cephotaxim* or cepuroxim* 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 gentamytex or gentapuls 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 peniciline or pentids or pentrex 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 sagestem* 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 vancostacin or vancin or vancom* or vancomycin* or vankom* or velosef or vetramox* or vicillin 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 emezd
91	88 not 90
92	82 or 85
93	91 and 92 [SR/RCT data]
94	91 not 93 [Non-RCT data]

1

2

**Database(s): Cochrane Library – Wiley interface**

3

**Cochrane Database of Systematic Reviews**, Issue 11 of 12, November 2022, **Cochrane**

4

**Central Register of Controlled Trials**, Issue 11 of 12, November 2022

5

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	((abocillin 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 ceftriaxon* or cefuroxim* or cefzil or cepazin* or cephalosporin* or cephotaxim* or cephuoxim* 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 permepen or pfizerpen or polycillin or polymox or polymyxin* or primafen or pricipen 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 vancocostacin 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

6

7

**Database(s): Database of Abstracts of Reviews of Effects (DARE); HTA Database –**

8

**CRD interface**

9

Date of last search: 12 February 2021

#	Searches
1	MeSH DESCRIPTOR meningitis IN DARE,HTA



#	Searches
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	(((abbocillin 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 ceftriaxon* or cefepim* or cefixim* or cefizox or cefobid* or cefotan or cefotaxim* or ceftin or ceftriaxon* or ceftriazon* or cefuroxim* or ceftzil 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 peniciline 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 vancocostacin 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

1  
2

1

2 **Economic Search**

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

4

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

7 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 pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or GBS or streptococcus pneumon* or s pneumon*) NEAR3 (septic* or sepsis* or bacter?emi?))) IN NHSEED, HTA
12	((meningoencephalitis* 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 meningococemia*)) 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

8

9 **Database(s): Medline & Embase (Multifile) – OVID interface**10 **Embase Classic+Embase 1947 to 2022 November 09, Ovid MEDLINE(R) and Epub**11 **Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to November**  
12 **09, 2022**

13 Date of last search: 10 November 2022

14 *Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of*  
15 *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 Meningococemia/ 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

#	Searches
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
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	(multiattribute* 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.

#	Searches
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.
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

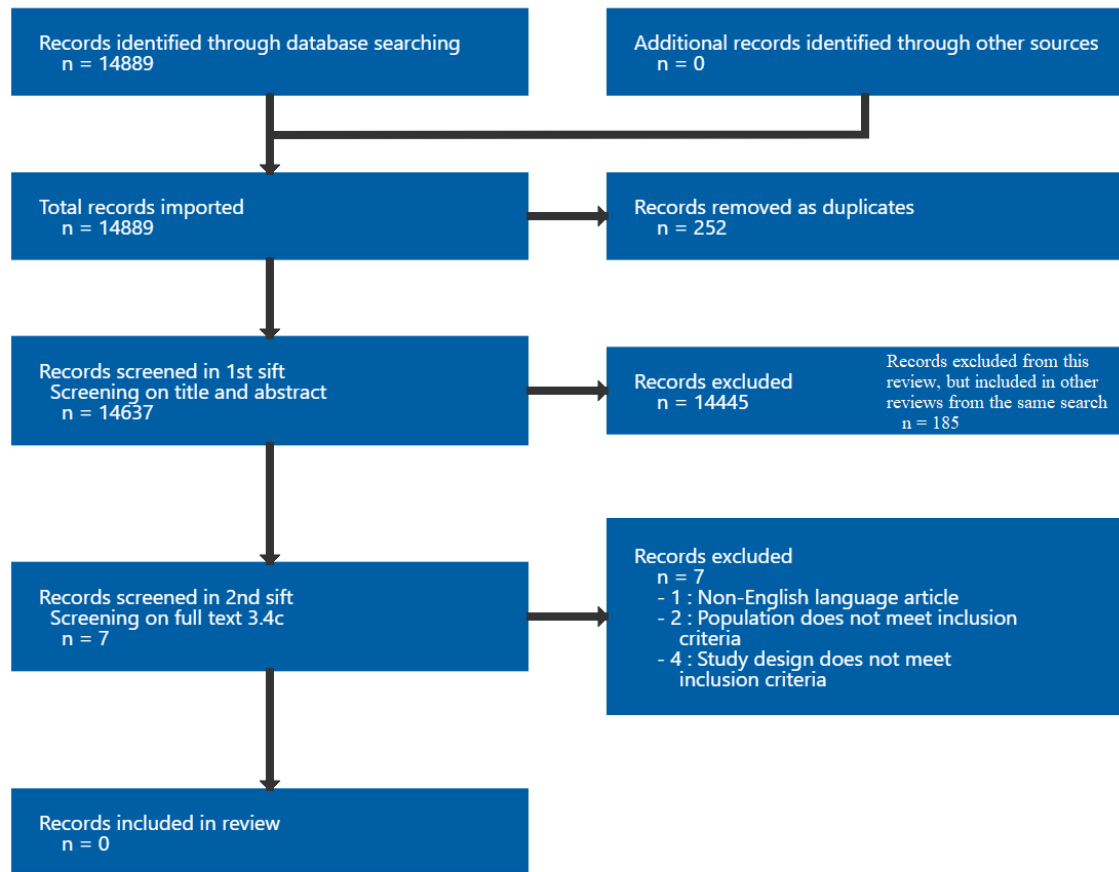
1

2

# 1 Appendix C Effectiveness evidence study selection

## 2 Study selection for: What antibiotic treatment regimens are effective in treating 3 bacterial meningitis caused by Group B streptococcus?

4 Figure 1: Study selection flow chart



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1 **Appendix D Evidence tables**

2 **Evidence tables for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused**  
3 **by Group B streptococcus?**

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

5

## 1 **Appendix E Forest plots**

### 2 **Forest plots for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by** 3 **Group B streptococcus?**

4 No meta-analysis was conducted for this review question and so there are no forest plots.

1

## 2 **Appendix F GRADE tables**

3 **GRADE tables for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused**  
4 **by Group B streptococcus?**

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

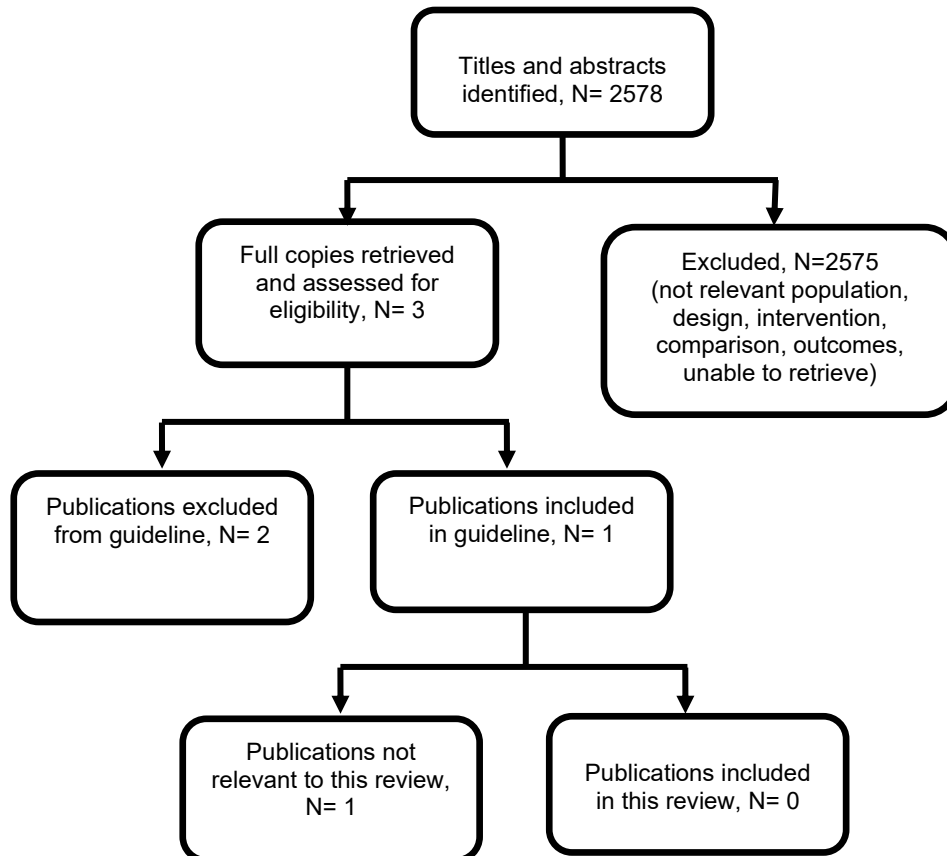


1 **Appendix G Economic evidence study selection**

2 **Study selection for: What antibiotic treatment regimens are effective in treating**  
3 **bacterial meningitis caused by Group B streptococcus?**

4 **Figure 2: Study selection flow chart**

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1 **Appendix H Economic evidence tables**

2 **Economic evidence tables for review question: What antibiotic treatment**  
3 **regimens are effective in treating bacterial meningitis caused by Group B**  
4 **streptococcus?**

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

6

- 1 **Appendix I Economic model**
- 2 **Economic model for review question: What antibiotic treatment regimens are**
- 3 **effective in treating bacterial meningitis caused by Group B streptococcus?**
- 4 No economic analysis was conducted for this review question.

1

## 2 Appendix J Excluded studies

3 **Excluded studies for review question: What antibiotic treatment regimens are**  
 4 **effective in treating bacterial meningitis caused by Group B streptococcus?**

### 5 Excluded effectiveness studies

6 The excluded studies table only lists the studies that were considered and then excluded at  
 7 the full-text stage for this review (N=7) and not studies (N=185) that were considered and  
 8 then excluded from the search at the full-text stage as per the PRISMA diagram in Appendix  
 9 C for the other review questions in the same search.

10 **Table 3: Excluded studies and reasons for their exclusion**

Study	Code [Reason]
de Louvois, J.; Mulhall, A.; Hurley, R. (1982) Cefuroxime in the treatment of neonates. Archives of disease in childhood 57(1): 59-62	Study design does not meet inclusion criteria
Fister, Petja, Pecek, Jerneja, Jeverica, Samo et al. (2022) Neonatal Group B Streptococcal Meningitis: Predictors for Poor Neurologic Outcome at 18 Months. Journal of child neurology 37(1): 64-72	Study design does not meet inclusion criteria
Lim, S. Y. and Miller, J. L. (2020) Ampicillin Dose for Early and Late-Onset Group B Streptococcal Disease in Neonates. American Journal of Perinatology	Study design does not meet inclusion criteria
Roine, I., Ledermann, W., Foncea, L. M. et al. (2000) Randomized trial of four vs. seven days of ceftriaxone treatment for bacterial meningitis in children with rapid initial recovery. Pediatric infectious disease journal 19(3): 219-222	Population 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
Tauzin, M., Ouldali, N., Levy, C. et al. (2019) Combination therapy with ciprofloxacin and third-generation cephalosporin versus third-generation cephalosporin monotherapy in Escherichia coli meningitis in infants: a multicentre propensity score-matched observational study. Clinical Microbiology and Infection 25(8): 1006-1012	Population does not meet inclusion criteria
Wang, Wenhui, Han, Hong, Du, Lijun et al. (2022) Clinical Features and Outcomes of Streptococcus pneumoniae Meningitis in Children: A Retrospective Analysis of 26 Cases in China. Neuropediatrics 53(1): 32-38	Study design does not meet inclusion criteria

11

1 **Excluded economic studies**

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

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1 **Appendix K Research recommendations – full details**

2 **Research recommendations for review question: What antibiotic treatment**  
3 **regimens are effective in treating bacterial meningitis caused by Group B**  
4 **streptococcus?**

5 No research recommendation was made for this review.