

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

[E5] Evidence review for antibiotics for bacterial meningitis caused by *Listeria monocytogenes*

NICE guideline number tbc

Evidence review underpinning recommendations 1.6.14 and 1.6.16 in the NICE guideline

September 2023

Draft for consultation

This evidence review was developed by NICE

Disclaimer

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

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Contents

Antibiotics for bacterial meningitis caused by <i>Listeria monocytogenes</i>	6
Review question	6
Introduction	6
Summary of the protocol	6
Methods and process	7
Effectiveness evidence.....	7
Summary of included studies.....	8
Summary of the evidence.....	8
Economic evidence	8
Economic model.....	8
The committee’s discussion and interpretation of the evidence	8
Recommendations supported by this evidence review	10
References – included studies.....	11
Appendices	12
Appendix A Review protocols	12
Review protocol for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by <i>Listeria monocytogenes</i> ?.....	12
Appendix B Literature search strategies	22
Literature search strategies for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused <i>Listeria monocytogenes</i> ?.....	22
Appendix C Effectiveness evidence study selection	29
Study selection for: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by <i>Listeria monocytogenes</i> ?	29
Appendix D Evidence tables	30
Evidence tables for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by <i>Listeria monocytogenes</i> ?.....	30
Appendix E Forest plots	31
Forest plots for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by <i>Listeria monocytogenes</i> ?.....	31
Appendix F GRADE tables	32
GRADE tables for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by <i>Listeria monocytogenes</i> ?.....	32
Appendix G Economic evidence study selection	33
Study selection for: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by <i>Listeria monocytogenes</i> ?	33
Appendix H Economic evidence tables	34
Economic evidence tables for review question: What antibiotic treatment	

	regimens are effective in treating bacterial meningitis caused by Listeria monocytogenes?	34
Appendix I	Economic model	35
	Economic model for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by Listeria monocytogenes?.....	35
Appendix J	Excluded studies	36
	Excluded studies for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by Listeria monocytogenes?.....	36
Appendix K	Research recommendations – full details.....	37
	Research recommendations for review question: What antibiotic treatment regimens are effective in treating bacterial meningitis caused by Listeria monocytogenes?	37

1 Antibiotics for bacterial meningitis caused 2 by *Listeria monocytogenes*

3 Review question

4 What antibiotic treatment regimens are effective in treating bacterial meningitis caused by
5 *Listeria monocytogenes*?

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. *Listeria*
9 *monocytogenes* is a rare cause of bacterial meningitis, usually seen in people at the
10 extremes of age or with significant underlying immunosuppression.

11 The aim of this review is to determine what antibiotic treatment regimens are effective in
12 treating bacterial meningitis caused by *Listeria monocytogenes*.

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)**

Population	All adults, young people, children and babies (excluding neonates defined as aged 28 days old and younger) with confirmed bacterial meningitis caused by <i>Listeria monocytogenes</i>
Intervention	Antibiotic agent of interest: <ul style="list-style-type: none">• Ampicillin• Amoxicillin• Benzylpenicillin sodium• Gentamicin• Amikacin• Meropenem• Linezolid• Co-trimoxazole
Comparison	Stage 1 (all antibiotic agents of interest): <ul style="list-style-type: none">• Antibiotic agent A (single or combination)* vs Antibiotic agent B (single or combination)* *Gentamycin and amikacin to be used in combination with other antibiotics. Stage 2 (antibiotic agents identified during stage 1 as most effective/for use where there are contraindications) Comparisons: <ul style="list-style-type: none">• 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 Population: adults, children and infants <ul style="list-style-type: none">• 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

	<p>deficits; measured from discharge up to 1 year after discharge)</p> <p>Population: adults</p> <ul style="list-style-type: none">• Functional impairment (measured by any validated scale at any time point) <p>Population: children and infants</p> <ul style="list-style-type: none">• 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) <p>Important</p> <p>Population: adults, children and infants</p> <ul style="list-style-type: none">• 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) <p>Population: adults</p> <ul style="list-style-type: none">• Intracranial collections as a complication (defined as abscess or empyema) <p>Population: children and infants</p> <ul style="list-style-type: none">• Functional impairment (measured by any validated scale at any time point) <p>*For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age.</p>
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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 meningitis
37 caused by *Listeria monocytogenes*, and the committee agreed that given the absence of
38 evidence the first line treatment recommended by the previous NICE guideline on meningitis
39 (NICE 2010) should be retained. The committee recommended intravenous amoxicillin or
40 ampicillin for 21 days for people with meningitis caused by *Listeria monocytogenes*. The

1 previous guideline recommendation only applied to children younger than 3 months, however
2 the committee agreed that the recommendation could be extended to cover all ages as
3 *Listeria monocytogenes* is also a common infective organism in older adults and there are
4 additional risk factors for *Listeria monocytogenes* which are not restricted to extremes of age
5 (pregnancy, malignancy, kidney disease, liver disease, diabetes, alcoholism, and
6 immunocompromising treatment). The committee agreed that there is no evidence that the
7 effectiveness of antibiotics in sterilising the cerebrospinal fluid (CSF) would be different in
8 adults and children. The committee acknowledged that there is some evidence that
9 antibiotics penetrate the CSF of very young children better than in older children and adults
10 because their blood-brain barriers are less intact, but, in the committee's experience, this
11 difference disappears when the meninges are inflamed; therefore, the committee would
12 expect the antibiotics to penetrate into the CSF equally well regardless of age in people with
13 bacterial meningitis.

14 The committee also recommended considering the addition of intravenous gentamicin or co-
15 trimoxazole for the first 7 days. The committee agreed that this should not happen routinely
16 as both antibiotics can be toxic and have additional monitoring requirements associated with
17 them; additionally, gentamicin does not penetrate well into CSF. However, they agreed that
18 combination therapy can be beneficial, especially where there is a bacteraemic or septic
19 component to the illness, but that it should only be done in consultation with an infection
20 specialist (a microbiologist or infectious diseases specialist) because of the associated risks
21 and monitoring requirements. The committee agreed that although gentamicin is more often
22 used as an addition to amoxicillin in current practice, co-trimoxazole would be more
23 appropriate for older adults due to a significant risk of nephrotoxicity with gentamicin. Where
24 gentamicin or co-trimoxazole are used, the committee agreed that they should only be used
25 during the first stage of treatment such as the first 7 days, as this is when they would be most
26 beneficial, and it would avoid using them longer than necessary due to risks associated with
27 renal function or other toxicity. The committee noted that this was an off-label use of co-
28 trimoxazole (in January 2024) and doses, frequency, and duration in the BNF (British
29 National Formulary 2023) and BNFC (British National Formulary for Children 2023) for
30 severe infections should be followed.

31 There was no evidence found on antibiotic use for meningitis caused by *Listeria*
32 *monocytogenes* in people with a penicillin allergy, but the committee agreed it was important
33 to make a recommendation for this population. The committee agreed that clinicians should
34 seek information about the nature of the allergy and advice from an infection specialist before
35 making a treatment decision. The committee acknowledged that it is important that treatment
36 is not delayed; however, they agreed that information about the nature of allergy is often
37 readily available from the patient's family. Given that amoxicillin and ampicillin are penicillin
38 antibiotics an alternative first line treatment was required. Based on their clinical knowledge
39 and experience, the committee agreed that cephalosporin-induced anaphylaxis is rare. The
40 committee recommended that ceftriaxone or cefotaxime should be considered if the nature of
41 the allergic reaction they get is non-anaphylactic or non-severe. They also recommended the
42 addition of co-trimoxazole (for 21 days). This is in line with [BNF advice](#) in the case of history
43 of hypersensitivity to penicillin for people with meningitis caused by *Listeria monocytogenes*.
44 If the allergic reaction is anaphylactic or severe, alternatives to ceftriaxone or cefotaxime will
45 be needed. The committee discussed that chloramphenicol is commonly used in the case of
46 severe beta-lactam (penicillin, amoxicillin, or cephalosporin) allergy. Based on clinical
47 knowledge and experience, the committee recommended chloramphenicol (in addition to co-
48 trimoxazole) for people with meningitis caused by *Listeria monocytogenes* and anaphylactic
49 or severe penicillin allergy.

50 Given that no evidence was identified for this review the committee discussed including a
51 research recommendation on the effectiveness of antibiotics for the treatment of meningitis
52 caused by *Listeria monocytogenes*. However, the committee agreed that given this condition
53 is very rare it would be unlikely that a clinical trial would be feasible.

1 **Cost effectiveness and resource use**

2 This review question was not prioritised for economic analysis and therefore the committee
3 made a qualitative assessment of the likely cost-effectiveness of their recommendations.
4 Given the absence of any evidence the committee retained the recommendations made by
5 the previous NICE guideline (NICE 2010) and therefore no significant resource impact is
6 anticipated.

7 **Recommendations supported by this evidence review**

8 This evidence review supports recommendations 1.6.14 and 1.6.16. Other evidence
9 supporting recommendation 1.6.16 can be found in evidence reviews on antibiotic regimens
10 for bacterial meningitis before or in the absence of identifying causative infecting organism
11 (see evidence reviews D1 to D3) and for specific causative organisms (see evidence reviews
12 E1 to E4, and E6).
13

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 **OtherNICE 2010**

8 National Institute for Health and Care Excellence (2010). Meningitis (bacterial) and
9 meningococcal septicaemia in under 16s: recognition, diagnosis and management [NICE
10 Clinical guideline No. CG102]. Available at: <https://www.nice.org.uk/guidance/cg102>
11 [Accessed on 2022 Apr 19]

12

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 *Listeria monocytogenes*?

5 **Table 2: Review protocol**

Field	Content
PROSPERO registration number	CRD42021276592
Review title	Antibiotics for bacterial meningitis caused by <i>Listeria monocytogenes</i>
Review question	What antibiotic treatment regimens are effective in treating bacterial meningitis caused by <i>Listeria monocytogenes</i> ?
Objective	This review aims to find out what is the optimal antibiotic treatment regimen in improving outcomes for people with bacterial meningitis caused by <i>Listeria monocytogenes</i>
Searches	<p>The following databases will be searched:</p> <ul style="list-style-type: none">• Cochrane Central Register of Controlled Trials (CENTRAL)• Cochrane Database of Systematic Reviews (CDSR)• Embase• MEDLINE <p>Searches will be restricted by:</p> <ul style="list-style-type: none">• Date limitations: 1980• English language• Human studies <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 <i>Listeria monocytogenes</i>
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 <i>Listeria monocytogenes</i></p> <p>Exclusion:</p> <p>People:</p> <ul style="list-style-type: none"> • 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	<p>Antibiotic agent of interest:</p> <ul style="list-style-type: none"> • Ampicillin • Amoxicillin • Benzylpenicillin sodium • Gentamicin • Amikacin • Meropenem • Linezolid • Co-trimoxazole
Comparator/Reference standard/Confounding factors	<p>Stage 1 (all antibiotic agents of interest):</p> <ul style="list-style-type: none"> • Antibiotic agent A (single or combination)* vs Antibiotic agent B (single or combination)* <p>*Gentamycin and amikacin to be used in combination with other antibiotics</p>

Field	Content
	<p>Stage 2 (antibiotic agents identified during stage 1 as most effective/for use where there are contraindications)</p> <p>Comparisons:</p> <ol style="list-style-type: none"> 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	<p>Include published full-text papers:</p> <ul style="list-style-type: none"> • Systematic reviews of RCTs • RCTs • If insufficient RCTs: prospective cohort studies • If insufficient prospective cohort studies: retrospective cohort studies <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"> • Co-morbidity • Severity of infection at presentation (including sepsis) <p>Exclude:</p> <ul style="list-style-type: none"> • Conference abstracts
Other exclusion criteria	<ul style="list-style-type: none"> • 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	<p>This guidance will fully update the following: Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (CG102)</p>
Primary outcomes (critical outcomes)	<p>Adults</p> <ul style="list-style-type: none"> • All-cause mortality (measured up to 1 year after discharge)

Field	Content
	<ul style="list-style-type: none"> • 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) • Functional impairment (measured by any validated scale at any time point) <p>Children and infants</p> <ul style="list-style-type: none"> • 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) <p>*For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age.</p>
Secondary outcomes (important outcomes)	<p>Adults</p> <ul style="list-style-type: none"> • 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). • Intracranial collections as a complication (defined as abscess or empyema) <p>Children and infants</p> <ul style="list-style-type: none"> • Hearing impairment (defined as any level of hearing impairment; measured from

Field	Content
	<p>discharge up to 1 year after discharge)</p> <ul style="list-style-type: none"> • 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 • CSF sterilisation (defined as treatment failure, time to sterilisation or delay)
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"> • 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 <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 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</p>

Field	Content
	<p>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 I^2 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: http://www.gradeworkinggroup.org/</p> <p>Minimally important differences:</p> <ul style="list-style-type: none"> • All-cause mortality: statistical significance • Serious intervention-related adverse effects: statistical significance • CSF sterilization: statistical significance • Intracranial collections: statistical significance • Validated scales: Published MIDs where available; if not GRADE default MIDs • All other outcomes: GRADE default MIDs
Analysis of sub-groups	<p>Evidence will be stratified by:</p> <p>Stage 1</p> <ul style="list-style-type: none"> • Age: <ul style="list-style-type: none"> ○ Younger Infants, older infants and children: >28 days to <18* years of age ○ Adults: ≥18* years of age <p>Stage 2</p> <ul style="list-style-type: none"> • Age: <ul style="list-style-type: none"> ○ Younger Infants: >28 days to ≤3 months of age ○ Older infants and children: >3 months to <18* years of age

Field	Content												
	<ul style="list-style-type: none"> ○ Adults: ≥18* years of age <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"> ● Age: <ul style="list-style-type: none"> ○ Young and middle aged adults ○ Older adults* <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> <ul style="list-style-type: none"> ● Women: <ul style="list-style-type: none"> ○ Pregnant women ○ Non-pregnant women <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"> <tbody> <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> </tbody> </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 checked="" type="checkbox"/>	Intervention												
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<input type="checkbox"/>	Prognostic												
<input type="checkbox"/>	Qualitative												
<input type="checkbox"/>	Epidemiologic												
<input type="checkbox"/>	Service Delivery												

Field	Content		
	<input type="checkbox"/>	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	<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	<p>Named contact: National Guideline Alliance</p> <p>Named contact e-mail: meningitis&meningococcal@nice.org.uk</p> <p>Organisational affiliation of the review: National Institute for Health and Care Excellence (NICE) and National Guideline Alliance</p>		
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		

Field	Content
	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=CRD42021276592
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"> • 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.
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	www.nice.org.uk

- 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:*
- 3 *minimally important difference; NICE: National Institute for Health and Care Excellence; PDI: psychomotor development index; PRESS: Peer Review of Electronic Search*
- 4 *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;*
- 5 *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 *Listeria* 4 *monocytogenes*? 5

6 This was a combined search to cover both this review and D1, D2, D3, E1, E2, E3 E4, 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 Clinical Search

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

15 Date of last search: 10 November 2022

16 *Multifile database codes: emczd = Embase Classic+Embase; ppez = MEDLINE(R) and Epub Ahead of*
 17 *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 benzy?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 cefzil or cepazim* 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

#	Searches
	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 pentrexl or pentrexyl or permapen or pfizerpen or polycillin or polymox or polymyxin* or primafen or principen or quinolon* or refobacin* or refobacin* or ribom?cin* or rifampicin or rifampin* or rocefallin or rocefin or rocephin* or roscillin or rifloxacin* 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).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
85	83 or 84

#	Searches
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 [SR/RCT data]
94	91 not 93 [Non-RCT data]

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2

Database(s): Cochrane Library – Wiley interface

3

Cochrane Database of Systematic Reviews, Issue 11 of 12, November 2022, **Cochrane Central Register of Controlled Trials**, Issue 11 of 12, November 2022

4

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	((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 ceftriaxon* 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 cristicillin 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 pentrelx or pentrexyl or permepen or pfizerpen or polycillin or polymox or polymyxin* or primaferen or principen or quinolon* or refobacin* or ribom?cin* or rifampicin or rifampin* or rocefalin or rocefim 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 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)):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 – CRD interface

8

9

Date of last search: 12 February 2021

#	Searches
1	MeSH DESCRIPTOR meningitis IN DARE,HTA
2	MeSH DESCRIPTOR meningitis, bacterial IN DARE,HTA

#	Searches
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	(((((meningoencephalitis* 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 meningococemia*)))) 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 cefatriaxon* or cefepim* or cefixim* or cefizox or cefobid* or cefotan or cefotaxim* or ceftin or ceftriaxon* or ceftriazon* or cefuroxim* or cezil 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 rocefen 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 vicillin 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

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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 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	((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

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15

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 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
19	Value of life/ use ppez

Meningitis (bacterial) and meningococcal disease: recognition, diagnosis and management: evidence reviews for antibiotics for bacterial meningitis caused by *Listeria monocytogenes* DRAFT (September 2023)

#	Searches
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 qol* or euroqol* or euro qol5d* or euroqol5d* 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

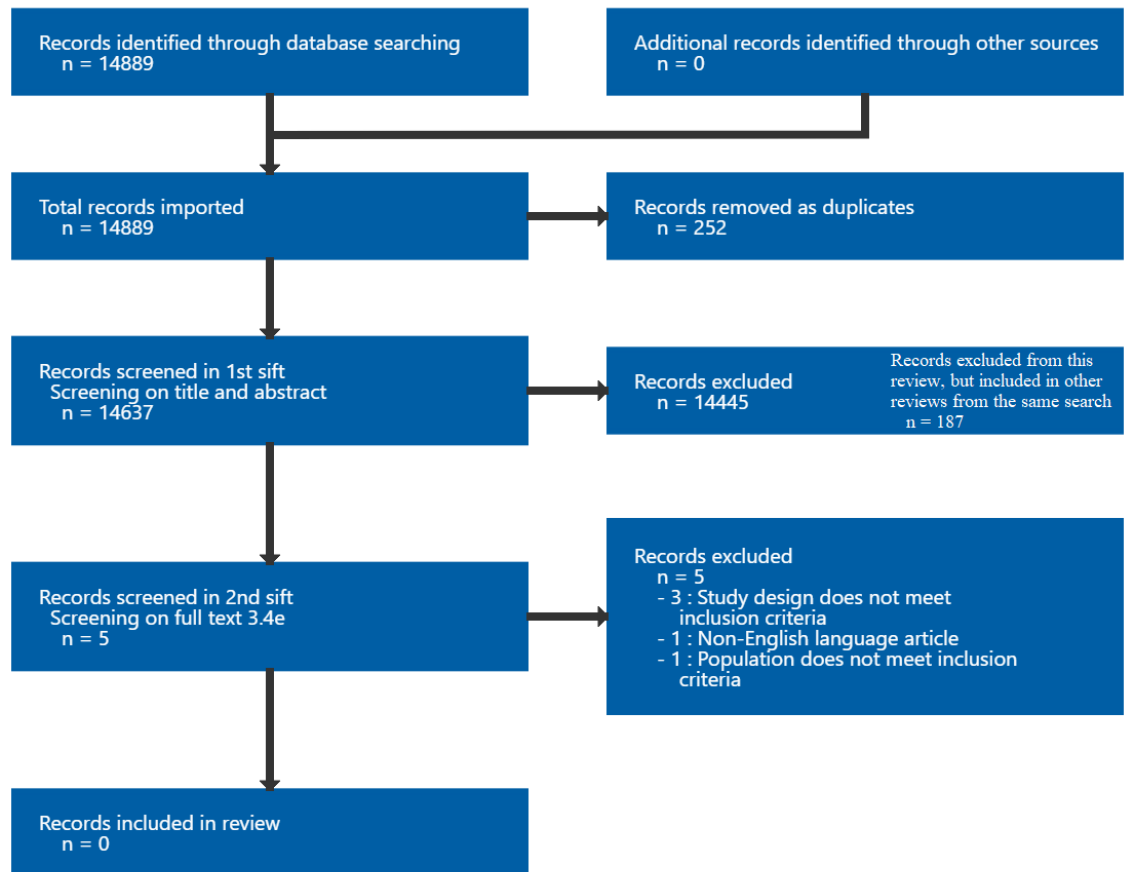
#	Searches
85	randomized controlled trial/ or random*.ti,ab.
86	84 not 85
87	animals/ not humans/
88	exp Animals, Laboratory/
89	exp Animal Experimentation/
90	exp Models, Animal/
91	exp Rodentia/
92	(rat or rats or mouse or mice).ti.
93	86 or 87 or 88 or 89 or 90 or 91 or 92
94	letter.pt. or letter/
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 *Listeria monocytogenes*?

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 *Listeria monocytogenes*?**

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 ***Listeria monocytogenes*?**
- 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 *Listeria monocytogenes*?**
- 5 No evidence was identified which was applicable to this review question.

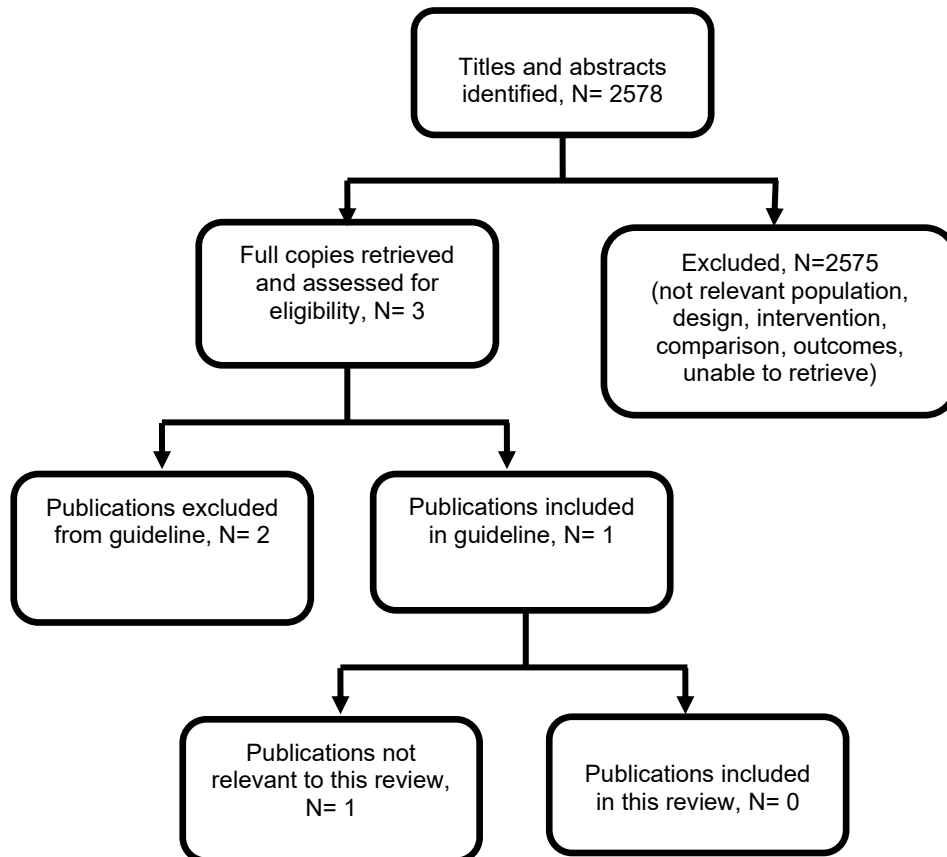
1 **Appendix G Economic evidence study selection**

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

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

6 **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 *Listeria***
4 ***monocytogenes*?**

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 *Listeria monocytogenes*?**

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 *Listeria monocytogenes*?**

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=5) and not studies (N=187) 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
Dzupova, O., Rozsypal, H., Smiskova, D. et al. (2013) <i>Listeria monocytogenes</i> meningitis in adults: The Czech Republic experience. BioMed Research International 2013: 846186	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
Thonnings, S., Knudsen, J. D., Schonheyder, H. C. et al. (2016) Antibiotic treatment and mortality in patients with <i>Listeria monocytogenes</i> meningitis or bacteraemia. Clinical Microbiology and Infection 22(8): 725-730	Study design does not meet inclusion criteria

11

12 **Excluded economic studies**

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

14

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 *Listeria***
4 ***monocytogenes*?**

5 No research recommendation was made for this review.