National Institute for Health and Care Excellence

Final

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

[B5] Evidence review for role of neuroimaging prior to lumbar puncture

NICE guideline NG240

Evidence review underpinning recommendations 1.4.6 to 1.4.8 in the NICE guideline

March 2024

Final

This evidence review was developed by NICE

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What is the role of neuroimaging prior to lumbar puncture?

Introduction

Bacterial meningitis is a rare but serious infection, which can occur in any age group. Early recognition of the condition requires a high index of suspicion.

Cerebrospinal fluid (CSF) investigations are crucial for the diagnosis of bacterial meningitis, and obtaining CSF samples for urgent investigation should be prioritised whenever a diagnosis of bacterial meningitis is being considered.

Neuroimaging is frequently performed prior to performing a lumbar puncture either to exclude other differential diagnoses or to assess for the presence of significantly raised intracranial pressure. However, obtaining neuroimaging in all cases of suspected bacterial meningitis delays performing a lumbar puncture and obtaining CSF for important diagnostic investigations. In turn, this may also delay effective treatment and management.

The aim of this review is to evaluate the role of neuroimaging prior to lumbar puncture when bacterial meningitis is suspected.

Summary of the protocol

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

Table 1: Summary of the protocol (PICO table)

Population	All adults, young people, children and babies (excluding neonates defined as aged 28 days old and younger) with suspected bacterial meningitis
Intervention	Lumbar puncture without prior neuroimaging
Comparison	Neuroimaging (CT or MRI) followed by lumbar puncture if appropriate (based on neuroimaging results)
Outcome	**Critical** Population: adults, infants and children • Brain herniation (may be reported as herniation, loss of pupillary reactivity, significant drop on Glasgow Coma Scale, coning) • All-cause mortality (measured up to 1 year after discharge) • Any long-term neurological impairment (defined as any motor deficits, sensory deficits, cognitive deficits*, or behavioural deficits*; measured from discharge up to 1 year after discharge) *For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age. **Important** Population: adults • Time between hospital admission and lumbar puncture • Time between hospital admission and starting antibiotics • 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 Population: infants and children • Time between hospital admission and lumbar puncture • Time between hospital admission and starting antibiotics • 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) • Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant

CT: computerised tomography; MDI: mental development index; MRI: magnetic resonance imaging; PDI: psychomotor development index; SD: standard deviation

For further details see the review protocol in appendix A.

Methods and process

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

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

Effectiveness evidence

Included studies

Three cohort studies were included for this review: 2 prospective cohort studies (Glimaker 2018, Hasbun 2001) and 1 retrospective cohort study (Glimaker 2015). No relevant test and treat randomised controlled trials were identified.

The included studies are summarised in Table 2.

All studies compared lumbar puncture without prior computerised tomography (CT) with lumbar puncture after CT in adults only. Only 1 study provided adjustment for confounding factors for relevant outcomes (Glimaker 2018).

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

Excluded studies

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

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies.

Study	Population	Intervention	Comparison	Outcomes	Comments
Glimaker 2015	N=712 Adults	Lumbar puncture without prior	Lumbar puncture with prior CT	• All-cause mortality • Any long-term	The study reported adjusting for

Study	Population	Intervention	Comparison	Outcomes	Comments
Retrospective cohort study Sweden	patients with acute community - acquired bacterial meningitis Age, Median (range): 61 (17 to 95) Patients with immunocompromised state: NR	CT No further details reported	No further details reported	neurological impairment (defined as neurological and/ or hearing deficits) • Time between hospital admission and starting antibiotics • Absence of functional impairment (defined as recovery to normal activity without neurological or hearing deficits)	confounding factors but did not report adjusted estimates for the relevant outcomes.
Glimaker 2018 Prospective cohort Sweden	N=815 Adults (age >16 years) with acute bacterial meningitis Age, Median (IQR): 62 (48 to 70) Patients with immunocompromised state: 38%	Lumbar puncture without prior CT No further details reported	Lumbar puncture with prior CT No further details reported	• All-cause mortality • Any long-term neurological impairment (arm/leg drift; cranial nerve palsy) • Time between hospital admission and starting antibiotics (adequate treatment with antibiotics and corticosteriods <1 hour; <2 hours) • Absence of functional impairment (defined as GOS 5 and no neurological sequelae or hearing deficit)	Confounding factors were adjusted for (sex, age, immunocompromised state, typical symptoms, mental status, new-onset seizures, cranial nerve palsy, septic shock, and causative organism) for outcomes, except for neurological deficit outcomes.
Hasbun 2001 Prospective Cohort study USA	N=301 Adults >16 years with suspected meningitis	Lumbar puncture without prior CT No further details reported	Lumbar puncture with prior CT No further details reported	• Time between hospital admission and lumbar puncture • Time between hospital admission and	No adjustment for confounding factors

Study	Population	Intervention	Comparison	Outcomes	Comments
	Age, Median (IQR), years: 40 (18 to 93)			starting antibiotics	

CT: computerised tomography; GOS: Glasgow outcome scale; IQR: interquartile range

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Summary of the evidence

This section is a narrative summary of the findings of the review, as presented in the GRADE tables in appendix F. For details of the committee's confidence in the evidence and how this affected recommendations, see The committee's discussion and interpretation of the evidence.

The evidence was assessed as being moderate to very low quality, most of the studies at very high risk of bias due to not adjusting analyses for confounding factors, seriously indirect due to a significant proportion of the population being immunosuppressed, and seriously imprecise findings. There was insufficient evidence to stratify by age or according to risk factors for brain herniation. See the GRADE tables in appendix F for the certainty of the evidence for each individual outcome.

Compared with lumbar puncture after CT, lumbar puncture without prior CT had lower rates of mortality, long term neurological impairment in the form of neurological and/or hearing deficits, time to antibiotic treatment (with or without corticosteroids) within 1 hour and within 2 hours, and a higher rate of people with no functional impairment, in adults with bacterial meningitis. However, there was no important difference observed in the evidence reviewed for long term neurological deficits in the form of cranial nerve palsy and arm/leg drift. The findings were seriously or very seriously imprecise for these outcomes, except for absence of functional impairment; therefore, they should not be taken as definitive evidence of association, or lack of association.

It was not possible to estimate the 95% confidence intervals for the mean difference on time to lumbar puncture and time to starting antibiotics in Hasbun 2001, as standard deviations and the number of patients in each arm were not reported, respectively.

No studies reported data for the other outcomes in the protocol (brain herniation, severe developmental delay, or serious intervention-related adverse effects), and no evidence was available for babies and children.

See appendix F for full GRADE tables.

Economic evidence

Included studies

A single economic search was undertaken for all topics included in the scope of this guideline, but no economic studies were identified which were applicable to this review question. See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Economic model

No economic modelling was undertaken for this review because, although this question was originally prioritised, the clinical evidence although limited suggested that cost-effectiveness using the reviewed data would be self-evident and that original economic analysis would simply reinforce any recommendations made on the clinical evidence alone.

Unit costs

Resource	Unit costs	Source
Computerised Tomography Scan of One Area, without Contrast, 19 years and over	£99	National Schedule of NHS Costs 2020-21 [1]
Computerised Tomography Scan of One Area, without Contrast, between 6 and 18 years	£198	National Schedule of NHS Costs 2020-21 [2]
Computerised Tomography Scan of One Area, without Contrast, 5 years and under	£92	National Schedule of NHS Costs 2020-21 [3]
Magnetic Resonance Imaging Scan of One Area, without Contrast, 19 years and over	£176	National Schedule of NHS Costs 2020-21 [4]
Magnetic Resonance Imaging Scan of One Area, without Contrast, between 6 and 18 years	£272	National Schedule of NHS Costs 2020-21 [5]
Magnetic Resonance Imaging Scan of One Area, without Contrast, 5 years and under	£281	National Schedule of NHS Costs 2020-21 [6]

[1] *Currency code RD20A*
[2] *Currency code RD20B*
[3] *Currency code RD20C*
[4] *Currency code RD01A*
[5] *Currency code RD01B*
[6] *Currency code RD01C*

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Brain herniation can occur following a lumbar puncture if there is raised intracranial pressure. As this is a potentially life-threatening complication, brain herniation and mortality were selected as critical outcomes due to the potential for neuroimaging to identify raised intracranial pressure and indirectly reduce the risk of brain herniation by impacting the decision to perform a lumbar puncture. Long-term neurological impairment was also prioritised as a critical outcome as it can be a complication of both brain herniation and meningitis itself.

Time between hospital admission and 1) lumbar puncture and 2) starting antibiotics were included as important outcomes due to concerns from the committee that the time required for neuroimaging can cause delays in both of these, which may have a detrimental effect on outcomes. As with long-term neurological impairment, functional impairment may be a complication of both brain herniation and meningitis itself, so it was selected as an important outcome in adults. However, severe developmental delay was included as an important outcome for children as this may be more commonly reported than neurological and functional impairment in trials of young children. Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant was also included as an important outcome to identify serious adverse effects other than brain herniation, for example, medically significant bleeding.

The quality of the evidence

The quality of the evidence was assessed with GRADE methodology and was rated as moderate quality for the absence of functional impairment outcome due to the population being indirect (including people who were immunocompromised), and low to very low quality for the remaining outcomes due to high risk of bias (arising from lack of adjustment for confounding factors), the population being indirect, and imprecision (due to wide confidence intervals and small number of events).

No evidence was found that reported on brain herniation, severe developmental delay or serious intervention-related adverse effects leading to death, disability or hospitalisation.

Benefits and harms

The committee considered the evidence comparing outcomes for people who underwent lumbar puncture without prior computerised tomography (CT) relative to those who underwent lumbar puncture with prior CT. Lumbar puncture without prior CT reduced mortality compared with lumbar puncture performed after neuroimaging. Lumbar puncture without prior CT was also associated with lower rates of neurological and/or hearing deficits and functional impairment, and a shorter time to antibiotic treatment (with or without corticosteroids), relative to lumbar puncture after CT. These findings were consistent with the clinical expertise of the committee, and they agreed that neuroimaging should not be routinely performed before lumbar puncture.

No evidence was identified for the critical outcome of brain herniation. Based on their clinical knowledge and experience, the committee recognised the potential for neuroimaging to identify raised intracranial pressure and indirectly reduce the risk of brain herniation by impacting the decision to perform a lumbar puncture. Based on evidence from the review on factors associated with brain herniation (see evidence review B4) and their knowledge and experience, the committee agreed that there are specific instances when imaging should be performed before lumbar puncture to mitigate the risk of brain herniation, namely when a person shows recognised signs of raised intracranial pressure (new focal neurological features, abnormal pupillary reactions, a Glasgow coma scale score of 9 or less, or a progressive and sustained or rapid fall in level of consciousness). The committee also agreed that imaging should be performed prior to lumbar puncture where the person has risk factors for an evolving space-occupying lesion. However, the committee discussed that neuroimaging should not cause a delay to management of bacterial meningitis and thus recommended that a blood sample should be taken, antibiotics should be started, and the person should be stabilised before imaging.

Cost effectiveness and resource use

No original economic analysis was undertaken for this review question and therefore the committee made a qualitative assessment of the likely cost-effectiveness of their recommendations.

The committee recognised that undertaking neuroimaging prior to lumbar puncture would increase costs by introducing a diagnostic investigation into the pathway which, as well as delaying optimal treatment for bacterial meningitis, would often provide little or no information that would improve subsequent management. Whilst the committee were aware that much of the evidence reviewed was of low quality, because of a high risk of bias, they did note that neuroimaging prior to lumbar puncture was associated with poorer outcomes having a significant impact on health-related quality of life. Therefore, the committee considered that it was reasonable to conclude that neuroimaging prior to LP was not cost-effective for people with suspected bacterial meningitis, where prompt appropriate antibiotics are critical to favourable outcomes.

Notwithstanding the limitations of the evidence, the committee were aware that their recommendations were consistent with other international guidance as well as recommendations made in previous NICE guidance. However, the committee noted that poor adherence with guidelines has been observed in the US, UK, the Netherlands, and Sweden (Salazar 2017, Ellis 2022, Costerus 2016, Glimaker 2018). A recent retrospective cohort study in the UK (Ellis 2022) in a population with community acquired meningitis, found that neuroimaging prior to lumbar puncture occurred in 94% of patients, even though the majority of these (83%) had no contraindication to lumbar puncture. Less than 1% of patients had lumbar puncture within the first hour after arrival at hospital and only 26% had lumbar puncture within the first 8 hours. The study authors remarked that delays in obtaining CSF is associated with worse pathogen detection, more exposure to unnecessary anti-infectives, increased hospital length of stay and increased mortality. They concluded that “in most

cases, brain imaging is not indicated in adults with suspected community-acquired meningitis; however, in our cohort, a significant number of patients had unnecessary scans. Although complications following LP are rare, there may be an unfounded fear of cerebral herniation following LP, even in those with no clinical features of brain shift, which is leading to excessive use of imaging."

In addition to overcaution with respect to brain herniation, the committee also discussed other factors as to why compliance with guidelines might be poor. They noted that clinical assessment often takes place in a busy emergency department which they thought would not always be conducive to lumbar puncture and where there may be incentives in terms of patient workflow management from providing CT first, as that can facilitate faster patient outflows from the emergency department. The committee noted that the numbers presenting was also quite small which could limit the opportunities to learn from experience. The committee believed that logistically it was easier for LP to be performed quickly on a medical ward and that the time from admission to lumbar puncture would be improved if patients could be moved from the emergency department to an acute medical ward more quickly. The committee recognised that bed capacity could be a major implementation obstacle to this. The committee considered that the availability of LP kits could also be a limiting factor. Equipment shortages and lack of training were also factors picked up in a questionnaire (Defres 2015) considering possible barriers to timely LP. The committee noted that generating requests for all the tests required on a cerebrospinal fluid sample is laborious, and that sometimes tests are inadvertently omitted. It was suggested that electronic order sets could improve practice in this regard.

The committee believed that their recommendations made it clearer that neuroimaging should not be routinely undertaken. Whilst the recommendations do not substantively change current guidance the committee recognised that current practice is varied and often sub-optimal. The committee believed that widespread implementation of their recommendations has the potential to be cost saving to the NHS reducing unnecessary tests, ineffective treatments and hospital stay.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.4.6 to 1.4.8. Other evidence supporting the recommendations can be found in the evidence review on factors associated with brain herniation (see evidence review B4).

References – included studies

Effectiveness

Glimaker 2015

Glimaker, M., Johansson, B., Grindborg, O., Bottai, M., Lindquist, L., Sjolin, J., Adult bacterial meningitis: earlier treatment and improved outcome following guideline revision promoting prompt lumbar puncture, Clinical Infectious DiseasesClin Infect Dis, 60, 1162-9, 2015

Glimaker 2018

Glimaker, M., Sjolin, J., Akesson, S., Naucler, P., Lumbar Puncture Performed Promptly or After Neuroimaging in Acute Bacterial Meningitis in Adults: A Prospective National Cohort Study Evaluating Different Guidelines, Clinical Infectious DiseasesClin Infect Dis, 66, 321-328, 2018

Hasbun 2001

Hasbun, R., Abrahams, J., Jekel, J., Quagliarello, V. J., Computed tomography of the head before lumbar puncture in adults with suspected meningitis, New England Journal of Medicine, 345, 1727-1733, 2001

Economic

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

Other

Costerus 2016

Costerus, JM., Brouwer, MC., Bijlsma, MW., Tanck, MW., van der Ende, A., van de Beek, D. Impact of an evidence-based guideline on the management of community-acquired bacterial meningitis: a prospective cohort study. Clin Microbiol Infect 2016; 22:928–33.

Defres 2015

Defres, S., Mayer, J., Backman, R., et al. Performing lumbar punctures for suspected CNS infections: experience and practice of trainee doctors. Br J Hosp Med 2015;76:658–62.

Ellis 2022

Ellis, J., Harvey, D., Defres, S., et al. Clinical management of community acquired meningitis in adults in the UK and Ireland in 2017: a retrospective cohort study on behalf of the National Infection Trainees Collaborative for Audit and Research (NITCAR). BMJ Open 2022;12: e062698. doi:10.1136/bmjopen-2022-062698

Salazar 2017

Salazar, L., Hasbun, R,. Cranial imaging before lumbar puncture in adults with community-acquired meningitis: clinical utility and adherence to the Infectious Diseases Society of America guidelines. Clin Infect Dis 2017; 64:1657–62

Appendices

Appendix A Review protocols

Review protocol for review question: What is the role of neuroimaging prior to lumbar puncture?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42021245999
Review title	Role of neuro-imaging prior to lumbar puncture
Review question	What is the role of neuroimaging prior to lumbar puncture?
Objective	To evaluate the role of neuro-imaging prior to lumbar puncture
Searches	The following databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Database of Systematic Reviews (CDSR) Embase MEDLINE Searches will be restricted by: Date limitations: 1980 English language Human studies The full search strategies for MEDLINE database will be published in the final review. For each search, the principal database search strategy is quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist.
Condition or domain being studied	Suspected bacterial meningitis
Population	Inclusion: All adults, young people, children and babies (excluding neonates defined as aged 28 days old and

Field	Content
	younger) with suspected bacterial meningitis Exclusion: People: • with known immunodeficiency. • who have brain tumours, pre-existing hydrocephalus, intracranial shunts, previous neurosurgical procedures, or known cranial or spinal anomalies that increase the risk of bacterial meningitis. • with confirmed viral meningitis or viral encephalitis. • with confirmed tuberculous meningitis. • with confirmed fungal meningitis.
Intervention	Lumbar puncture without prior neuroimaging
Comparator	Neuroimaging (CT or MRI) followed by lumbar puncture if appropriate (based on neuroimaging results)
Types of study to be included	Include published full-text papers: • Systematic reviews of test-and-treat RCTs • Test-and-treat RCTs • If insufficient test-and-treat RCTs: prospective cohort studies • If insufficient prospective cohort studies: retrospective cohort studies Non-randomised studies will be downgraded for risk of bias if they do not adequately adjust for the following covariates, but will not be excluded for this reason: • Co-morbidity • Severity of illness at presentation • Antibiotics administered pre or post lumbar puncture • Infective organism Conference abstracts will not be considered.
Other exclusion criteria	Countries other than OECD high-income countries. Studies conducted prior to 1980 as CT scanning was not available before this date.

Field	Content
	Studies published not in English-language
Context	This guidance will fully update the following: Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (CG102)
Primary outcomes (critical outcomes)	Population: adults • Brain herniation (may be reported as herniation, loss of pupillary reactivity, significant drop on Glasgow Coma Scale, coning) • All-cause mortality (measured up to 1 year after discharge) • Any long-term neurological impairment (defined as any motor deficits, sensory deficits, cognitive deficits, or behavioural deficits; measured from discharge up to 1 year after discharge) Population: infants and children • Brain herniation (may be reported as herniation, loss of pupillary reactivity, significant drop on Glasgow Coma Scale, coning) • All-cause mortality (measured up to 1 year after discharge) • Any long-term neurological impairment (defined as any motor deficits, sensory deficits, cognitive deficits*, or behavioural deficits*; measured from discharge up to 1 year after discharge) *For infants and children below school-age, cognitive and behavioural deficits will be assessed at school-age.
Secondary outcomes (important outcomes)	Population: adults • Time between hospital admission and lumbar puncture • Time between hospital admission and starting antibiotics • 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 Population: infants and children • Time between hospital admission and lumbar puncture • Time between hospital admission and starting antibiotics • Severe developmental delay (defined as score of >2 SD below normal on validated assessment scales, or MDI or

Field	Content
	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) • Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation or that are life threatening or otherwise considered medically significant
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. 5% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs and quasi-RCTs • Cochrane ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where multiple studies report on the same outcome for the same comparison, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios if possible or odds ratios when required (for example if only available in this form in included studies) for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed by visual inspection of the forest plots and consideration of the I2 statistic. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled if the random effects model does not adequately address heterogeneity. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by

Field	Content
	the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences:** • Brain herniation: statistical significance • All-cause mortality: statistical significance • Time between hospital admission and lumbar puncture: statistical significance • Time between hospital admission and starting antibiotics: statistical significance • Serious intervention-related adverse effects leading to death, disability or prolonged hospitalisation: statistical significance • Validated scales: Published MIDs where available; if not GRADE default MIDs • All other outcomes: GRADE default MIDs
Analysis of sub-groups	Evidence will be stratified by: Age: • Younger and older Infants: >28 days to <1 year of age • Children: ≥1 year to <18* years of age • Adults: ≥18* years of age Risk factors for brain herniation: • Present • Absent *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. Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes: Age: • Young and middle aged adults • Older adults*

Field	Content			
	Neurodisability: • Present • Absent *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. 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.			
Type and method of review	☒	Intervention		
	☐	Diagnostic		
	☐	Prognostic		
	☐	Qualitative		
	☐	Epidemiologic		
	☐	Service Delivery		
	☐	Other (please specify)		
Language	English			
Country	England			
Anticipated or actual start date	11/03/2021			
Anticipated completion date	07/12/2023			
Stage of review at time of this submission	Review stage		Started	Completed
	Preliminary searches		☑	☑
	Piloting of the study selection process		☑	☑
	Formal screening of search results		☑	☑

Field	Content		
	against eligibility criteria		
	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
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 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=CRD42021245999		
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard		

Field	Content	
	approaches such as: notifying registered stakeholders of publication publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
Keywords	Bacterial meningitis, lumbar puncture, brain herniation, neuro-imaging, CT, MRI	
Details of existing review of same topic by same authors	None	
Current review status	☐	Ongoing
	☒	Completed but not published
	☐	Completed and published
	☐	Completed, published and being updated
	☐	Discontinued
Additional information	None	
Details of final publication	www.nice.org.uk	

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CT: computerised tomography; GRADE: Grading of Recommendations Assessment, Development and Evaluation; MDI: mental development index; MID: minimally important difference; MRI: magnetic resonance imaging; NICE: National Institute for Health and Care Excellence; OECD: organisation for economic co-operation and development; PDI: psychomotor development index; PRESS: peer review of electronic search strategies; RCT: randomised controlled trial; RoB: risk of bias; ROBINS-I: risk of bias in non-randomised studies – of interventions; ROBIS: risk of bias in systematic reviews;

Appendix B Literature search strategies

Literature search strategies for review question: What is the role of neuroimaging prior to lumbar puncture?

Clinical Search

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

#	Searches
1	Meningitis/ or Meningitis, Bacterial/ or Meningitis, Escherichia Coli/ or Meningitis, Haemophilus/ or Meningitis, Listeria/ or Meningitis, Meningococcal/ or Meningitis, Pneumococcal/ or Meningoencephalitis/
2	1 use ppez
3	meningitis/ or bacterial meningitis/ or haemophilus meningitis/ or hemophilus influenzae meningitis/ or listeria meningitis/ or meningococcal meningitis/ or pneumococcal meningitis/ or meningoencephalitis/
4	3 use emczd
5	((bacter* or infect*) adj3 (meningit* or meninges* or leptomeninges* or subarachnoid space?)).ti,ab.
6	(meningit* adj3 (e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon* or septic* or sepsis* or bacter?emi?)).ti,ab.
7	((e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon*) adj3 (septic* or sepsis* or bacter?emi?)).ti,ab.
8	(meningit* or mening?encephalitis* 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	(Spinal Puncture/ or Punctures/) use ppez
14	(lumbar puncture/ or puncture/) use emczd
15	((spin* or lumbar* or dural* or thecal*) adj3 (punctur* or tap*)).ti,ab.
16	LP.ti,ab.
17	or/13-16
18	Neuroimaging/ or Diagnostic Imaging/ or exp tomography, emission-computed/ or tomography, x-ray computed/ or exp magnetic resonance imaging/
19	18 use ppez
20	neuroimaging/ or diagnostic imaging/ or exp computer assisted tomography/ or exp nuclear magnetic resonance imaging/
21	20 use emczd
22	neuroimaging.ti,ab.
23	diagnos* imag*.ti,ab.
24	((comput* or CT* or CAT* or emission or radionuclide) adj2 (imag* or scan* or tomogra*)).ti,ab.
25	magnetic resonance.ti,ab.
26	(MRI or MR* or NMR*).ti,ab.
27	(MR adj2 (imag* or scan* or spectroscop* or tomogra* or elastogra* or examin*)).ti,ab.
28	(magnet* adj2 (imag* or spectroscop* or tomogra* or scan* or elastogra* or examin*)).ti,ab.
29	or/19,21-28
30	12 and 17 and 29
31	Time Factors/ use ppez
32	therapy delay/ use emczd
33	time to treatment/ use emczd
34	((treatment* or therapy) adj3 delay*).ti,ab.
35	31 or 32 or 33 or 34
36	12 and 17 and 35
37	((time or timing or delay* or late* or earl* or soon*) adj3 (spin* or lumbar* or dural* or thecal*) adj3 (punctur* or tap*)).ti,ab.
38	((time or timing or delay* or late* or earl* or soon*) adj3 LP).ti,ab.
39	37 or 38
40	12 and 39
41	30 or 36 or 40
42	((letter/ or editorial/ or news/ or exp historical article/ or anecdotes as topic/ or comment/ or case report/ or (letter or comment*).ti.) not (randomized controlled trial/ or random*.ti,ab.)) or (animals not humans).sh. or exp animals,

#	Searches
	laboratory/ or exp animal experimentation/ or exp models, animal/ or exp rodentia/ or (rat or rats or mouse or mice).ti.
43	42 use ppez
44	((letter.pt. or letter/ or note.pt. or editorial.pt. or case report/ or case study/ or (letter or comment*).ti.) not (randomized controlled trial/ or random*.ti,ab.)) or ((animal/ not human/) or nonhuman/ or exp animal experiment/ or exp experimental animal/ or animal model/ or exp rodent/ or (rat or rats or mouse or mice).ti.)
45	44 use emczd
46	43 or 45
47	41 not 46
48	limit 47 to English language

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

#	Searches
#1	MeSH descriptor: [Meningitis] this term only
#2	MeSH descriptor: [Meningitis, Bacterial] this term only
#3	MeSH descriptor: [Meningitis, Escherichia coli] this term only
#4	MeSH descriptor: [Meningitis, Haemophilus] this term only
#5	MeSH descriptor: [Meningitis, Listeria] this term only
#6	MeSH descriptor: [Meningitis, Meningococcal] this term only
#7	MeSH descriptor: [Meningitis, Pneumococcal] this term only
#8	MeSH descriptor: [Meningoencephalitis] this term only
#9	MeSH descriptor: [Neisseria meningitidis] explode all trees
#10	((bacter* or infect*) near/3 (mening* or leptomening* or subarachnoid space*)):ti,ab,kw
#11	(("e coli" or "escherichia coli" or haemophilus or hemophilus or hib or (h next influenz*) or listeria* or pneumococc* or (gram next negativ* next bacill*) or streptococc* or GBS or (s next pneumon*)) near/3 (septic* or sepsis* or bacteraemi* or bacteremi* or infect*)):ti,ab,kw
#12	(meningit* or mening?encephalitis* or (mening* next encephalitis*)).:ti,ab,kw
#13	((neisseria* next mening*) or (n next mening*)):ti,ab,kw
#14	MeSH descriptor: [Meningococcal Infections] this term only
#15	meningococc*:ti,ab,kw
#16	{or #1-#15}
#17	MeSH descriptor: [Spinal Puncture] this term only
#18	MeSH descriptor: [Punctures] this term only
#19	(((spin* or lumbar* or dural* or thecal*) near/3 (punctur* or tap*))):ti,ab,kw
#20	(LP):ti,ab,kw
#21	{or #17-#20}
#22	MeSH descriptor: [Neuroimaging] this term only
#23	MeSH descriptor: [Diagnostic Imaging] this term only
#24	MeSH descriptor: [Tomography, Emission-Computed] explode all trees
#25	MeSH descriptor: [Tomography, X-Ray Computed] this term only
#26	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#27	(neuroimag* or "neuro imag*"):ti,ab,kw
#28	(diagnos* next imag*):ti,ab,kw
#29	(((comput* or CT* or CAT* or emission or radionuclide) near/2 (imag* or scan* or tomogra*))):ti,ab,kw
#30	(magnetic next resonance):ti,ab,kw
#31	((MRI or MR* or NMR*)):ti,ab,kw
#32	((MR near/2 (imag* or scan* or spectroscop* or tomogra* or elastogra* or examin*))):ti,ab,kw
#33	((magnet* near/2 (imag* or spectroscop* or tomogra* or scan* or elastogra* or examin*))):ti,ab,kw
#34	{or #22-#33}
#35	#16 and #21 and #34
#36	MeSH descriptor: [Time Factors] this term only
#37	(((treat* or therap*) near/3 delay*)):ti,ab,kw
#38	#36 or #37
#39	#16 and #21 and #38
#40	(((time or timing or delay* or late* or earl* or soon*) near/3 (spin* or lumbar* or dural* or thecal*) near/3 (punctur* or tap*))):ti,ab,kw
#41	(((time or timing or delay* or late* or earl* or soon*) near/3 LP)):ti,ab,kw
#42	#40 or #41
#43	#16 and #42
#44	#35 or #39 or #43
#45	"conference":pt or (clinicaltrials or trialsearch):so
#46	#44 not #45

Database(s): Database of Abstracts of Reviews of Effects (DARE); HTA Database – CRD interface
Date of last search: 19 April 2021

#	Searches
1	MeSH DESCRIPTOR Spinal Puncture IN DARE,HTA
2	(((spin* or lumbar* or dural* or thecal*) NEAR3 (punctur* or tap*))) IN DARE, HTA
3	(LP) IN DARE, HTA
4	#1 OR #2 OR #3
5	MeSH DESCRIPTOR Neuroimaging IN DARE,HTA
6	MeSH DESCRIPTOR Diagnostic Imaging IN DARE,HTA
7	MeSH DESCRIPTOR tomography, emission-computed EXPLODE ALL TREES IN DARE,HTA
8	MeSH DESCRIPTOR tomography, x-ray computed IN DARE,HTA
9	MeSH DESCRIPTOR magnetic resonance imaging EXPLODE ALL TREES IN DARE,HTA
10	(neuroimaging) IN DARE, HTA
11	(diagnos* NEXT imag*) IN DARE, HTA
12	(((comput* or CT* or CAT* or emission or radionuclide) NEAR2 (imag* or scan* or tomogra*))) IN DARE, HTA
13	(magnetic NEXT resonance) IN DARE, HTA
14	((MRI or MR* or NMR*)) IN DARE, HTA
15	((MR NEAR2 (imag* or scan* or spectroscop* or tomogra* or elastogra* or examin*))) IN DARE, HTA
16	((magnet* NEAR2 (imag* or spectroscop* or tomogra* or scan* or elastogra* or examin*))) IN DARE, HTA
17	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
18	#4 AND #17
19	MeSH DESCRIPTOR Time Factors IN DARE,HTA
20	(((treatment* or therapy) NEAR3 delay*)) IN DARE, HTA
21	#19 OR #20
22	#4 AND #21
23	(((time or timing or delay* or late* or earl* or soon*) NEAR3 (spin* or lumbar* or dural* or thecal*) NEAR3 (punctur* or tap*))) IN DARE, HTA
24	(((time or timing or delay* or late* or earl* or soon*) NEAR3 LP)) IN DARE, HTA
25	#18 OR #22 OR #23 OR #24

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	((meningencephalitis* or meningoencephalitis* or meningit*)) IN NHSEED, HTA
13	MeSH DESCRIPTOR Meningococcal Infections IN NHSEED,HTA
14	MeSH DESCRIPTOR Neisseria meningitidis EXPLODE ALL TREES IN NHSEED,HTA
15	((meningococc* NEAR3 (sepsis* or septic* or toxic* or endotoxic* or disease* or infection*))) IN NHSEED, HTA
16	((meningococcus* or meningococci* or meningococcaemia* or meningococcemia*)) IN NHSEED, HTA
17	((Neisseria* NEXT mening*)) IN NHSEED, HTA
18	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17

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

Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

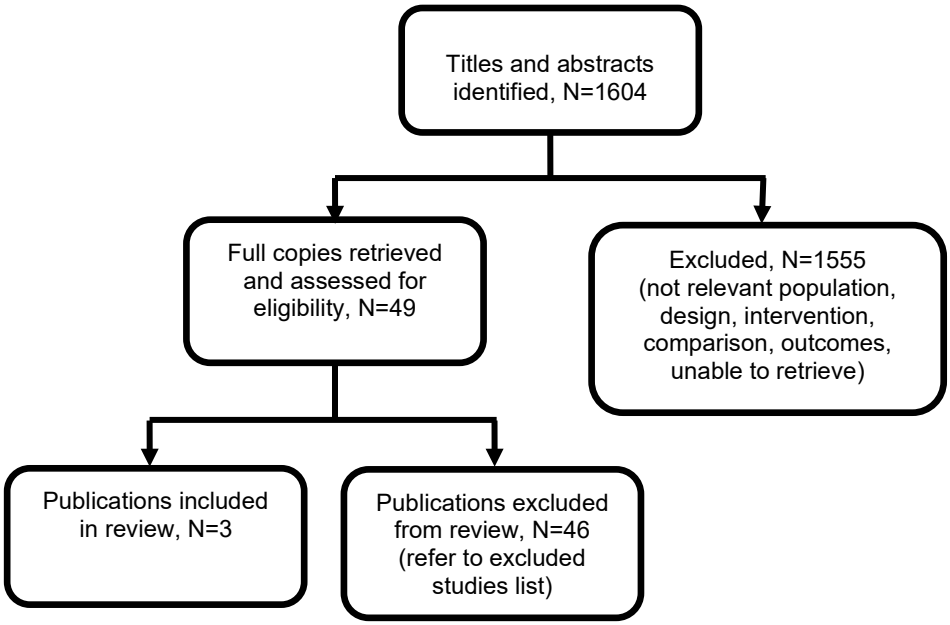
#	Searches
1	Meningitis/ or Meningitis, Bacterial/ or Meningitis, Escherichia Coli/ or Meningitis, Haemophilus/ or Meningitis, Listeria/ or Meningitis, Meningococcal/ or Meningitis, Pneumococcal/ or Meningoencephalitis/
2	1 use ppez
3	meningitis/ or bacterial meningitis/ or haemophilus meningitis/ or listeria meningitis/ or pneumococcal meningitis/ or meningoencephalitis/
4	3 use emczd
5	((bacter* or infect*) adj3 (meningit* or meninges* or leptomeninges* or subarachnoid space?)).ti,ab.
6	(meningit* adj3 (e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon* or septic* or sepsis* or bacter?emi?)).ti,ab.
7	((e coli or escherichia coli or h?emophilus or hib or h?emophilus influenz* or h influenz* or listeria* or meningococc* or pneumococc* or gram-negativ* bacill* or gram negativ* bacill* or streptococc* or group B streptococc* or GBS or streptococcus pneumon* or s pneumon*) adj3 (septic* or sepsis* or bacter?emi?)).ti,ab.
8	(mening?encephalitis* or meningit*).ti,ab.
9	or/2,4-8
10	Meningococcal Infections/ or exp Neisseria meningitidis/
11	10 use ppez
12	Meningococcosis/ or Meningococcemia/ or Neisseria Meningitidis/
13	12 use emczd
14	(meningococc* adj3 (sepsis* or septic* or toxic* or endotoxic* or disease? or infection?)).ti,ab.
15	(meningococcus* or meningococci* or meningococc?emi?).ti,ab.
16	(Neisseria* mening* or n mening*).ti,ab.
17	or/11,13-16
18	Economics/ use ppez
19	Value of life/ use ppez
20	exp "Costs and Cost Analysis"/ use ppez
21	exp Economics, Hospital/ use ppez
22	exp Economics, Medical/ use ppez
23	Economics, Nursing/ use ppez
24	Economics, Pharmaceutical/ use ppez
25	exp "Fees and Charges"/ use ppez
26	exp Budgets/ use ppez
27	health economics/ use emczd
28	exp economic evaluation/ use emczd
29	exp health care cost/ use emczd
30	exp fee/ use emczd
31	budget/ use emczd
32	funding/ use emczd
33	budget*.ti,ab.
34	cost*.ti.
35	(economic* or pharmaco?economic*).ti.
36	(price* or pricing*).ti,ab.
37	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38	(financ* or fee or fees).ti,ab.
39	(value adj2 (money or monetary)).ti,ab.
40	or/18-39
41	Quality-Adjusted Life Years/ use ppez
42	Sickness Impact Profile/
43	quality adjusted life year/ use emczd
44	"quality of life index"/ use emczd
45	(quality adjusted or quality adjusted life year*).tw.
46	(qaly* or qal or qald* or qale* or qtime* or qwb* or daly).tw.
47	(illness state* or health state*).tw.
48	(hui or hui2 or hui3).tw.
49	(multiattibute* or multi attribute*).tw.
50	(utilit* adj3 (score*1 or valu* or health* or cost* or measur* or disease* or mean or gain or gains or index*)).tw.
51	utilities.tw.
52	(eq-5d* or eq5d* or eq-5* or eq5* or euroqual* or euro qual* or euroqual 5d* or euro qual 5d* or euro qol* or euroqol*or euro quol* or euroquol* or euro quol5d* or euroquol5d* or eur qol* or eurqol* or eur qol5d* or eurqol5d* or eur?qul* or eur?qul5d* or euro* quality of life or european qol).tw.
53	(euro* adj3 (5 d* or 5d* or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).tw.
54	(sf36 or sf 36 or sf thirty six or sf thirtysix).tw.
55	(time trade off*1 or time tradeoff*1 or tto or timetradeoff*1).tw.
56	Quality of Life/ and ((quality of life or qol) adj (score*1 or measure*1)).tw.
57	Quality of Life/ and ec.fs.
58	Quality of Life/ and (health adj3 status).tw.
59	(quality of life or qol).tw. and Cost-Benefit Analysis/ use ppez
60	(quality of life or qol).tw. and cost benefit analysis/ use emczd
61	((qol or hrqol or quality of life).tw. or *quality of life/) and ((qol or hrqol* or quality of life) adj2 (increas* or decreas* or

#	Searches
	improv* or declin* or reduc* or high* or low* or effect or effects or worse or score or scores or change*1 or impact*1 or impacted or deteriorat*)).ab.
62	Cost-Benefit Analysis/ use ppez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
63	cost benefit analysis/ use emczd and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
64	*quality of life/ and (quality of life or qol).ti.
65	quality of life/ and ((quality of life or qol) adj3 (improv* or chang*)).tw.
66	quality of life/ and health-related quality of life.tw.
67	Models, Economic/ use ppez
68	economic model/ use emczd
69	care-related quality of life.tw,kw.
70	((capability$ or capability-based$) adj (measure$ or index or instrument$)).tw,kw.
71	social care outcome$.tw,kw.
72	(social care and (utility or utilities)).tw,kw.
73	or/41-72
74	(9 or 17) and 40
75	(9 or 17) and 73
76	letter/
77	editorial/
78	news/
79	exp historical article/
80	Anecdotes as Topic/
81	comment/
82	case report/
83	(letter or comment*).ti.
84	76 or 77 or 78 or 79 or 80 or 81 or 82 or 83
85	randomized controlled trial/ or random*.ti,ab.
86	84 not 85
87	animals/ not humans/
88	exp Animals, Laboratory/
89	exp Animal Experimentation/
90	exp Models, Animal/
91	exp Rodentia/
92	(rat or rats or mouse or mice).ti.
93	86 or 87 or 88 or 89 or 90 or 91 or 92
94	letter.pt. or letter/
95	note.pt.
96	editorial.pt.
97	case report/ or case study/
98	(letter or comment*).ti.
99	94 or 95 or 96 or 97 or 98
100	randomized controlled trial/ or random*.ti,ab.
101	99 not 100
102	animal/ not human/
103	nonhuman/
104	exp Animal Experiment/
105	exp Experimental Animal/
106	animal model/
107	exp Rodent/
108	(rat or rats or mouse or mice).ti.
109	101 or 102 or 103 or 104 or 105 or 106 or 107 or 108
110	93 use ppez
111	109 use emczd
112	110 or 111
113	74 not 112
114	limit 113 to English language
115	75 not 112
116	limit 115 to English language
117	114 or 116

Appendix C Effectiveness evidence study selection

Study selection for review question: What is the role of neuroimaging prior to lumbar puncture?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What is the role of neuroimaging prior to lumbar puncture?

Table 4: Evidence tables – Effectiveness evidence

Study details	Results and risk of bias assessment using ROBINS-I
Full citation Glimaker, M., Johansson, B., Grindborg, O., Bottai, M., Lindquist, L., Sjolin, J., Adult bacterial meningitis: earlier treatment and improved outcome following guideline revision promoting prompt lumbar puncture, Clinical Infectious DiseasesClin Infect Dis, 60, 1162-9, 2015 **Ref Id** 1134726 **Country/ies where the study was carried out** Sweden **Study type** Retrospective cohort **Study dates** 2005 to 2012 **Inclusion criteria** Adults with acute community-acquired bacterial meningitis **Exclusion criteria** Not reported **Patient characteristics** N = 712 Sex, n (%) Female = 371 (52.1)	**Results** All cause mortality, n/N (%), p-value LP without prior CT = 6/178 (3.4), <0.01 LP after CT = 27/236 (11.4), <0.01 Any long-term neurological impairment (defined as neurological sequelae[1] and/or hearing deficits[2] at follow up 2-6 months after discharge) in survivors, n/N (%), p-value LP without prior CT = 32/151 (21.2), <0.01 LP after CT = 65/183 (35.5), <0.01 Time between hospital admission and starting antibiotics (Time from admission to adequate antibiotic treatment <1 hour), n/N (%) LP without prior CT = 60/154 (39) LP after CT = 47/189 (24.9) Time between hospital admission and starting antibiotics (Time from admission to adequate antibiotic treatment <2 hours), n/N (%), p-value LP without prior CT = 95/154 (61.7), <0.01 LP after CT = 91/189 (48.1), <0.05 Absence of functional impairment (defined as return to normal activity without neurological or hearing deficits at follow-up 2-6 months after discharge), n/N (%), p-value LP without prior CT = 119/157 (75.8), <0.001 LP after CT = 92/210 (43.8), <0.001 Study reported that adjustments were made but no adjusted data was

Study details	Results and risk of bias assessment using ROBINS-I
Male = 341 (47.9) Age, Median (range) = 61 (17 to 95) Causative organisms, n(%) Streptococcus pneumoniae = 361 (50.7) Neisseria meningitides = 86 (12.1) Haemophilus influenza = 47 (6.6) Listeria monocytogenes = 28 (3.9) Streptococcus spp. = 41 (5.8) Other bacteria = 64 (9.0) Unknown = 85 (11.9) Mental status on admission, n (%) RLS >2/GCS <12 = 215 (37.7) RLS ≤2/GCS ≥12 = 356 (62.3) Antibiotic treatment, n(%) Cefotaxime + Ampicillin = 296 (41.6) Cefotaxime = 126 (17.7) Meropenem = 214 (30.1) Other antibiotics = 76 (10.7) Corticosteroid treatment, n(%) Yes = 488 (75.0) **Interventions** Lumbar puncture without prior CT versus lumbar puncture with prior CT **Follow-up** 2 to 6 months	reported for the relevant outcomes [1] Neurological sequelae were specified as headache, cognitive dysfunction/dementia, vertigo or fatigue causing limitations of daily activity, epileptic seizures, ataxia, or persistent neurological deficits. [2] Hearing deficit/disability was defined by the patient as new onset of impairment, and audiometry was performed when appropriate. **1. Bias due to confounding (Low/Moderate/Serious/Critical/No information)** Serious - No adjustment for confounders for relevant outcomes **2. Bias in selection of participants into the study (Low/Moderate/Serious/Critical/No information)** Low - all eligible participants were included **3. Bias in classification of interventions (Low/Moderate/Serious/Critical/No information)** Moderate - intervention was recorded retrospectively **4. Bias due to deviations from intended interventions (Low/Moderate/Serious/Critical/No information)** Low - no deviations from intended intervention **5. Bias due to missing data (Low/Moderate/Serious/Critical/No information)** Low - analysis is likely to have removed bias from missing data **6. Bias in measurement of outcomes (Low/Moderate/Serious/Critical/No information)** Low - outcome was assessed in the same manner across groups **7. Bias in selection of the reported result (Low/Moderate/Serious/Critical/No information)** Low - reported results are based on statistical analysis plan

Study details	Results and risk of bias assessment using ROBINS-I
	Overall risk of bias (Low/Moderate/Serious/Critical/No information) Serious - one serious domain **Source of funding** Research and Development Funds from the Karolinska and Uppsala University Hospitals
Full citation Glimaker, M., Sjolin, J., Akesson, S., Naucler, P., Lumbar Puncture Performed Promptly or After Neuroimaging in Acute Bacterial Meningitis in Adults: A Prospective National Cohort Study Evaluating Different Guidelines, Clinical Infectious DiseasesClin Infect Dis, 66, 321-328, 2018 **Ref Id** 1134727 **Country/ies where the study was carried out** Sweden **Study type** Prospective cohort **Study dates** January 2008 to December 2015 **Inclusion criteria** Adults with acute bacterial meningitis (age >16 years) who were prospectively registered in the national Swedish quality register for ABM **Exclusion criteria** Not reported **Patient characteristics**	**Results** All-cause mortality, n/N (%) LP done without prior CT = 14/323 (4%) LP done after CT = 37/378 (10%) p<0.001 aOR (95% CI)= 0.38 (0.18 to 0.77) Any long-term neurological impairment, at follow-up 2-6 months after discharge, n/N (%) Arm/leg drift LP done without prior CT = 16/323 (5%) LP done after CT = 26/378 (6.9) p=0.28 Cranial nerve palsy LP done without prior CT = 10/323 (3.1) LP done after CT = 22/378 (5.8) p=0.09 Time between hospital admission and starting antibiotics (adequate treatment with antibiotics and corticosteriods <1 hour), n/N (%) LP done without prior CT =80/277 (29) LP done after CT = 60/328 (18), p=0.002 aOR (95% CI)= 2.46 (1.60 to 3.79) Time between hospital admission and starting antibiotics (Adequate treatment with antibiotics and corticosteroids <2 hours), n/N (%) LP done without prior CT = 113/277 (41)

Study details	Results and risk of bias assessment using ROBINS-I
N = 815 Age, Median (IQR), years = 62 (48 to 70) Male, n = 417 Female, n = 398 Immunocompromised state, n(%) Severe = 87 (10.7) Moderate = 225 (27.6) Total = 312 (38.3) Primary focus of infection, n(%) Ear, sinus, or lungs = 397 (48.7) Pharynx = 54 (6.6) Other/unknown = 364 (44.7) Triad of fever, headache, and neck stiffness = 232 (28.5) 86 (26.6) 109 (28.8) .52 Mental status (n = 780), n(%) RLS 1 = 300 (38.5) RLS 2–3 = 356 (45.6) RLS 4–8 = 124 (15.9) New-onset seizures, n(%) = 59 (7.2) Neurological deficit, n(%) Arm/leg drift = 45 (5.5) Cranial nerve palsy = 37 (4.5) Septic shock = 64 (7.9) Causative organism: Streptococcus pneumonia = 420 (51.5) Neisseria meningitides = 87 (10.7) Other bacteria = 232 (28.5) Unidentified etiology = 76 (9.3) Time from admission to adequate antibiotic and corticosteroid treatment (n = 700), n(%) <1 hour = 168 (24.0)	LP done after CT = 98/328 (30) p=0.005 aOR (95% CI)= 2.12 (1.45 to 3.10) Absence of functional impairment (defined as GOS 5 and no neurological sequelae[1] or hearing deficits[2]) at follow-up 2-6 months after discharge, n/N (%) LP done without prior CT = 169/274 (62) LP done after CT = 137/320 (43), p<0.001 aOR (95% CI)= 2.11 (1.47 to 3.00) [1] Neurological sequelae were specified as cognitive dysfunction/dementia, vertigo, epileptic seizures, ataxia, or persistent neurological deficits as defined by the clinician at the follow-up visit. [2] Hearing deficits was defined by the patient as new-onset of impairment and audiometry was performed when appropriate. **1. Bias due to confounding (Low/Moderate/Serious/Critical/No information)** Low –confounding factors were adjusted for (sex, age, immunocompromised state, typical symptoms, mental status, new-onset seizures, cranial nerve palsy, septic shock, and causative organism) **2. Bias in selection of participants into the study (Low/Moderate/Serious/Critical/No information)** Low - all eligible participants included **3. Bias in classification of interventions (Low/Moderate/Serious/Critical/No information)** Low - well defined intervention status **4. Bias due to deviations from intended interventions (Low/Moderate/Serious/Critical/No information)**

Study details	Results and risk of bias assessment using ROBINS-I
<2 hours = 252 (36.0) **Interventions** Lumbar puncture without CT versus lumbar puncture after CT **Follow-up** 2 to 6 months	Low - no deviations reported **5. Bias due to missing data (Low/Moderate/Serious/Critical/No information)** Low - no missing data reported **6. Bias in measurement of outcomes (Low/Moderate/Serious/Critical/No information)** Low - outcome adequately measured across groups **7. Bias in selection of the reported result (Low/Moderate/Serious/Critical/No information)** Low - results correspond to intended statistical analyses **Overall risk of bias (Low/Moderate/Serious/Critical/No information)** Low **Source of funding** Stockholm county council **Other information** Population is indirect with 312 (38.3%) patients being immunocompromised
Full citation Hasbun, R., Abrahams, J., Jekel, J., Quagliarello, V. J., Computed tomography of the head before lumbar puncture in adults with suspected meningitis, New England Journal of Medicine, 345, 1727-1733, 2001 **Ref Id** 1154110 **Country/ies where the study was carried out** USA	**Results** Time between hospital admission and lumbar puncture (Time from admission to emergency department to lumbar puncture), Mean (range), hours Patients who underwent CT before lumbar puncture = 5.3 (0.9 to 20.5) Patients who did not undergo CT before lumbar puncture = 3.0 (0.7 to 14.6) [p<0.001] Time between hospital admission and starting antibiotics (Time from

Study details	Results and risk of bias assessment using ROBINS-I
Study type Prospective cohort **Study dates** July 1995 to June 1999 **Inclusion criteria** Adults (persons aged 16 years and above) with suspected meningitis who were seen in the emergency department of Yale - New Haven Hospital, whether or not they underwent CT of the head before undergoing lumbar puncture. **Exclusion criteria** No pre-defined exclusion criteria. Patients were excluded after screening for the following reasons: • Identified in the emergency department after CT had been performed • Identified after they had been discharged from the emergency department • Did not undergo lumbar puncture despite having a normal result on the CT of the head • had undergone CT but scan was lost and result could not be verified by independent neuroradiologist • had been enrolled in the study during a previous episode • underwent CT before the collection of baseline data • underwent CT before arriving at emergency department • underwent CT for suspected stroke rather than suspected meningitis • declined to participate **Patient characteristics** Sample size (N) = 301 Sex n(%): Female = 166 (55) Male = 135 (45)	admission to emergency department to initiating empirical antibiotics therapy), Mean ± SD, hours Patients who underwent CT before lumbar puncture = 3.8 ± 2.9 Patients who did not undergo CT before lumbar puncture = 2.9 ± 2.0 [p = 0.09] **1. Bias due to confounding (Low/Moderate/Serious/Critical/No information)** Serious - No adjustment for confounding factors **2. Bias in selection of participants into the study (Low/Moderate/Serious/Critical/No information)** Low - Participants were selected on admission to the emergency department and followed up for 1 week after study entry **3. Bias in classification of interventions (Low/Moderate/Serious/Critical/No information)** Low - Intervention was clearly defined. **4. Bias due to deviations from intended interventions (Low/Moderate/Serious/Critical/No information)** Low - No deviations from intended interventions **5. Bias due to missing data (Low/Moderate/Serious/Critical/No information)** Low - no missing data **6. Bias in measurement of outcomes (Low/Moderate/Serious/Critical/No information)** Low - outcome measurement was comparable across groups and unlikely to be influenced by knowledge of the intervention **7. Bias in selection of the reported result (Low/Moderate/Serious/Critical/No information)** Moderate - there is no indication of selection of the reported results

Study details	Results and risk of bias assessment using ROBINS-I
Age, Median (IQR) = 40 (18 to 93) Age >/= 60 years [n(%)] = 47 (16) Symptoms at presentation, n(%): Headache = 239 (79) Fever = 202 (67) Photophobia = 149 (50) Stiff neck = 137 (46) Focal motor symptom = 27 (9) Focal sensory symptom 15(5) Seizure within 1 week before presentation = 21 (7) Signs and laboratory data at presentation, n(%) Temperature >100.4°F = 149 (50) Normal level of consciousness (Glasgow coma scale >13) = 274 (91) Papilledema = 1 (<1) >5 white cells/ml CSF = 80(27) Pathogen identified in CSF[1] = 18(6) Pathogen identified in blood[2] = 20(7) Neurologic findings, n(%) Alert = 256 (85) Answers 2 questions correctly = 249 (83) Follows 2 commands correctly = 260 (86) Gaze palsy = 7 (2) Abnormal visual fields = 7 (2) Facial palsy = 10 (3) Supranuclear = 8 (3) Peripheral = 2 (1) Arm drift = 25 (8) Leg drift = 37 (12) Limb ataxia = 5 (2)	**Overall risk of bias (Low/Moderate/Serious/Critical/No information)** Serious - one serious domain **Source of funding** No information **Other information** 75 patients (25%) were immunocompromised with HIV as the most common cause.

Study details	Results and risk of bias assessment using ROBINS-I
Abnormal sensation = 11 (4) Aphasia = 34 (11) Dysarthria = 36 (12) Extinction = 31 (10) n = 235 (78%) underwent CT before lumbar puncture n = 124 (41%) patients received empirical antibiotics [1]Pathogens identified in CSF include enterovirus in 8 patients, varicella-zoster virus in 1, Cryptococcus neoformans in 6, Neisseria meningitides in 2, and Streptococcus pneumonia in 1. [2]Pathogens identified in blood include Staphylococcus aureus in 3 patients, Strep. pneumonia in 4, Salmonella enterica serotype enteritidis in 3, enterococcus in 2, Escherichia coli in 2, C. neoformans in 2, veillonella in 1, coagulase-negative staphylococci in 1, group A streptococcus in 1 and group B streptococcus in 1 **Interventions** Lumbar puncture without prior CT versus lumbar puncture with prior CT **Follow-up** 1 week	

ABM: acute bacterial meningitis; aOR: adjusted odds ratio; CI: confidence interval; CT: computerised tomography; CSF: cerebrospinal fluid; GCS: Glasgow coma scale; GOS: Glasgow outcome scale; HIV: human immunodeficiency virus; IQR: interquartile range; LP: lumbar puncture; RLS: restless leg syndrome; SD: standard deviation

Appendix E Forest plots

Forest plots for review question: What is the role of neuroimaging prior to lumbar puncture?

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

Appendix F GRADE tables

GRADE tables for review question: What is the role of neuroimaging prior to lumbar puncture?

Table 5: Evidence profile for the comparison between lumbar puncture without prior CT versus lumbar puncture after CT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LP without prior CT	LP after CT	Relative (95% CI)	Absolute		
Mortality (adjusted analysis) (follow-up 2 to 6 months) - adults												
1 (Glimaker 2018)	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	very serious[2]	none	14/323 (4.3%)	37/378 (9.8%)	aOR 0.38 (0.18 to 0.8)	58 fewer per 1000 (from 18 fewer to 79 fewer)	VERY LOW	CRITICAL
Mortality (unadjusted analysis) (follow-up 2 to 6 months) – adults												
1 (Glimaker 2015)	observational studies	very serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/178 (3.4%)	27/236 (11.4%)	RR 0.29 (0.12 to 0.7)	81 fewer per 1000 (from 34 fewer to 101 fewer)	VERY LOW	CRITICAL
Any long term neurological impairment (unadjusted analysis) - cranial nerve palsy (follow-up 2 to 6 months) - adults												
1 (Glimaker 2018)	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	serious[4]	none	10/323 (3.1%)	22/378 (5.8%)	RR 0.53 (0.26 to 1.11)	27 fewer per 1000 (from 43 fewer to 6 more)	LOW	CRITICAL
Any long-term neurological impairment (unadjusted analysis) - arm/leg drift (follow-up 2 to 6 months) - adults												
1 (Glimaker 2018)	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	very serious[5]	none	16/323 (5%)	26/378 (6.9%)	RR 0.72 (0.39 to 1.32)	19 fewer per 1000 (from 42 fewer to 22 more)	VERY LOW	CRITICAL
Any long-term neurological impairment (unadjusted analysis) (defined as neurological and/ or hearing deficits) (follow-up 2 to 6 months)- adults												
1 (Glimaker 2015)	observational studies	very serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	32/151 (21.2%)	65/183 (35.5%)	RR 0.6 (0.41 to 0.86)	142 fewer per 1000 (from 50 fewer to 210	VERY LOW	CRITICAL

										fewer)		
Time from admission to lumbar puncture (follow-up 1 weeks; Better indicated by lower values) - adults												
1 (Hasbun 2001)	observational studies	very serious[3]	no serious inconsistency	serious[6]	NC	none	n=66 Mean (range) hours 3.0 (0.7 to 14.6)	n=235 Mean (range) hours 5.3 (0.9 to 20.5)	-	MD 2.3 higher (confidence interval NC) (p =<0.001)	VERY LOW	IMPORTANT
Time to antibiotic treatment <1 hour (unadjusted analysis) (follow-up 2 to 6 months) – adults												
1 (Glimaker 2015)	observational studies	very serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	60/154 (39%)	47/189 (24.9%)	RR 1.57 (1.14 to 2.15)	142 more per 1000 (from 35 more to 286 more)	VERY LOW	IMPORTANT
Time to antibiotics treatment <2 hours (unadjusted analysis) (follow-up 2 to 6 months) - adults												
1 (Glimaker 2015)	observational studies	very serious[3]	no serious inconsistency	no serious indirectness	serious[7]	none	95/154 (61.7%)	91/189 (48.1%)	RR 1.28 (1.06 to 1.55)	135 more per 1000 (from 29 more to 265 more)	VERY LOW	IMPORTANT
Adequate treatment with antibiotics and corticosteroids <1 hour (adjusted analysis) (follow-up 2 to 6 months) - adults												
1 (Glimaker 2018)	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	very serious[2]	none	80/277 (28.9%)	60/328 (18.3%)	aOR 2.46 (1.6 to 3.78)	172 more per 1000 (from 81 more to 275 more)	VERY LOW	IMPORTANT
Adequate treatment with antibiotics and corticosteroids <2 hours (adjusted analysis) (follow-up 2 to 6 months) - adults												
1 (Glimaker 2018)	observational studies	no serious risk of bias	no serious inconsistency	serious[6]	serious[7]	none	113/277 (40.8%)	98/328 (29.9%)	aOR 2.12 (1.45 to 3.1)	176 more per 1000 (from 83 more to 270 more)	LOW	IMPORTANT
Time from admission to initiating empirical antibiotics (follow-up 1 weeks; Better indicated by lower values) - adults												
1 (Hasbun 2001)	observational studies	very serious[3]	no serious inconsistency	serious[6]	NC	none	Mean (SD)[a] 2.9 ± 2.0	Mean (SD)[a] 3.8 ± 2.9	-	MD 0.9 higher (confidence interval NC) (p = 0.09)	VERY LOW	IMPORTANT
Absence of functional impairment (adjusted analysis) (defined as GOS 5 and no neurological sequelae or hearing deficit) (follow-up 2 to 6 months) - adults												

1 (Glimaker 2018)	observational studies	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	169/274 (61.7%)	137/320 (42.8%)	aOR 2.11 (1.47 to 3.03)	184 more per 1000 (from 96 more to 266 more)	MODERATE	CRITICAL
Absence of functional impairment (unadjusted analysis) (defined as recovery to normal activity without neurological or hearing deficits) (follow-up 2 to 6 months) - adults												
1 (Glimaker 2015)	observational studies	very serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	119/157 (75.8%)	92/210 (43.8%)	RR 1.73 (1.45 to 2.06)	320 more per 1000 (from 197 more to 464 more)	LOW	CRITICAL

aOR: adjusted odds ratio; CI: confidence interval; CT: computerised tomography; GOS: Glasgow outcome scale; LP: lumbar puncture; NC: not calculable; RR: risk ratio

[a] Number of patients not reported

[1] Population is indirect due to 38% of participants being immunocompromised

[2] <150 events

[3] Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I

[4] 95% CI crosses 1 MID

[5] 95% CI crosses 2 MIDs

[6] Population is indirect due to 25% of participants being immunocompromised

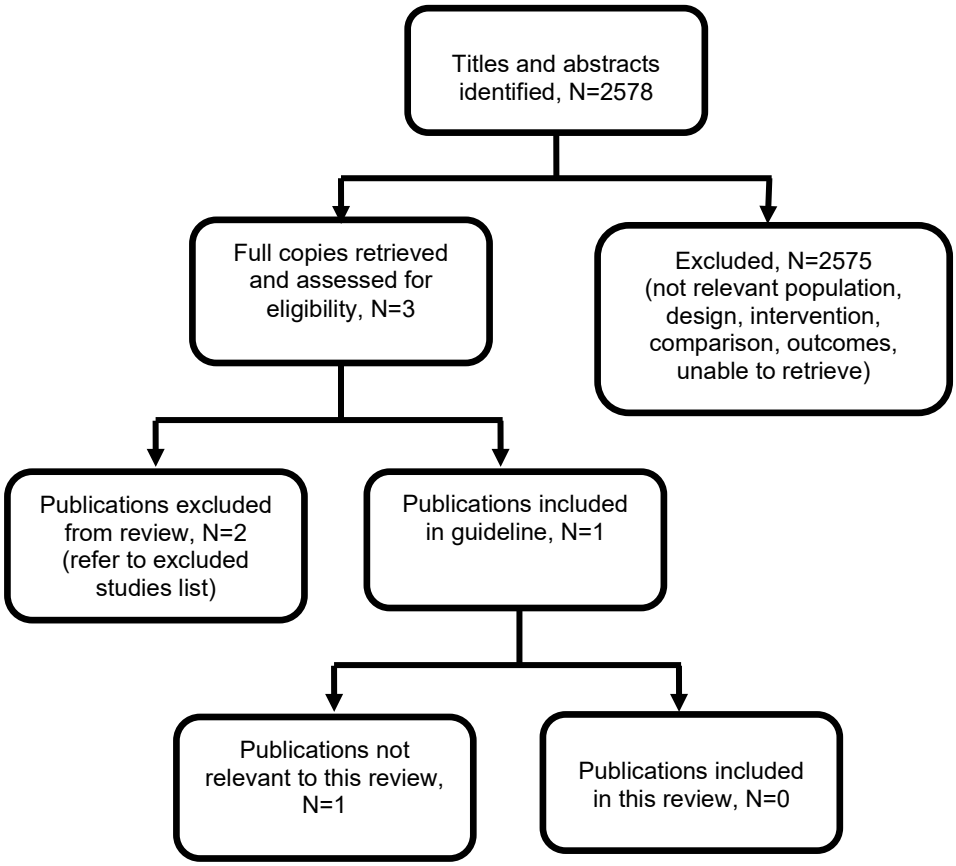
[7] <300 events

Appendix G Economic evidence study selection

Study selection for review question: What is the role of neuroimaging prior to lumbar puncture?

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

Figure 2: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What is the role of neuroimaging prior to lumbar puncture?

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

Appendix I Economic model

Economic model for review question: What is the role of neuroimaging prior to lumbar puncture?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What is the role of neuroimaging prior to lumbar puncture?

Excluded effectiveness studies

Table 6: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Allen, D. M., Computed tomography in suspected bacterial meningitis, Singapore Medical JournalSingapore Med J, 31, 196-197, 1990	Study design not of interest: narrative review
Anonymous,, To CT or not to CT before LP in the ED?, Hospital Practice, 35, 124, 2000	Participants not relevant to this review.
April, M. D., Long, B., Koyfman, A., Emergency Medicine Myths: Computed Tomography of the Head Prior to Lumbar Puncture in Adults with Suspected Bacterial Meningitis - Due Diligence or Antiquated Practice?, Journal of Emergency MedicineJ Emerg Med, 53, 313-321, 2017	Content of systematic review not relevant for this review question: most included studies did not report the comparison of interest. Of the two relevant included studies, one is already included in this review (Hasburn 2001) and the other only included participants who had CT.
Archer, B. D., Computed tomography before lumbar puncture in acute meningitis: a review of the risks and benefits, CMAJ Canadian Medical Association JournalCmaj, 148, 961-5, 1993	No relevant comparison for this review: no evidence presented comparing those who had lumbar puncture without prior neuroimaging and those who had neuroimaging followed by lumbar puncture if appropriate.
Aronin, S. I., Peduzzi, P., Quagliarello, V. J., Community-acquired bacterial meningitis: risk stratification for adverse clinical outcome and effect of antibiotic timing, Annals of Internal Medicine, 129, 862-9, 1998	No comparison of interest: study does not compare people who did nor did not have imaging.
Arroliga, A. C., Intensive care update: seven studies that should change your practice, Cleveland Clinic Journal of MedicineCleve Clin J Med, 69, 505-9, 2002	Study design not of interest for review: narrative commentary
Bhimraj, A., Acute community-acquired bacterial meningitis in adults: an evidence-based review, Cleveland Clinic Journal of MedicineCleve Clin J Med, 79, 393-400, 2012	Study design not of interest: narrative review
Bryan, C. S., Reynolds, K. L., Crout, L., Promptness of antibiotic therapy in acute bacterial meningitis, Annals of Emergency Medicine, 15, 544-547, 1986	No comparator of interest for review: no data presented to compare people who did or did not have imaging.
Bushore, M., Marante, A. A., Emergency Department stabilization of pediatric patients with bacterial meningitis: Current advances, Emergency Medicine Clinics of North America, 9, 239-250, 1991	Study design not of interest for review: narrative commentary
Chadwick, D. R., Lever, A. M., The impact of new diagnostic methodologies in the management of meningitis in adults at a teaching hospital, QjmQjm, 95, 663-70, 2002	No comparative data between neuroimaging prior to lumbar puncture versus no imaging prior to lumbar puncture.
Chaudhuri, A., Martin, P. M., Kennedy, P. G. E.,	Study questions not of interest for this review: no

Study	Reason for Exclusion
Andrew Seaton, R., Portegies, P., Bojar, M., Steiner, I., EFNS guideline on the management of community-acquired bacterial meningitis: Report of an EFNS Task Force on acute bacterial meningitis in older children and adults, European journal of neurology, 15, 649-659, 2008	data presented to assess brain imaging.
Choi, C., Bacterial meningitis in the elderly patient: Ten questions to consider, Infectious Diseases in Clinical Practice, 9, 17-22, 2000	Study design not of interest for review: narrative commentary
Costerus, J. M., Brouwer, M. C., Bijlsma, M. W., Tanck, M. W., van der Ende, A., van de Beek, D., Impact of an evidence-based guideline on the management of community-acquired bacterial meningitis: a prospective cohort study, Clinical Microbiology & InfectionClin Microbiol Infect, 22, 928-933, 2016	Study design not of interest for review: comparison between pre- and post-guideline practice.
Costerus, J. M., Brouwer, M. C., Bijlsma, M. W., van de Beek, D., Community-acquired bacterial meningitis, Current Opinion in Infectious DiseasesCurr Opin Infect Dis, 30, 135-141, 2017	Study design not of interest for review: narrative commentary
Costerus, J. M., Brouwer, M. C., Sprengers, M. E. S., Roosendaal, S. D., van der Ende, A., van de Beek, D., Cranial Computed Tomography, Lumbar Puncture, and Clinical Deterioration in Bacterial Meningitis: A Nationwide Cohort Study, Clinical infectious diseases, 67, 920-926, 2018	No relevant comparison for this review: 43/47 study participants and all matched controls had CT scans.
Costerus, J., Brouwer, M., Sprengers, M., Roosendaal, S., Van Der Ende, A., Van De Beek, D., Cerebral herniation after lumbar puncture in adults with bacterial meningitis, European Journal of Neurology, 24, 38, 2017	Conference Paper
Dyckhoff-Shen, S., Koedel, U., Pfister, H. W., Klein, M., SOP: emergency workup in patients with suspected acute bacterial meningitis, Neurological Research and Practice, 3, 2, 2021	Study design not of interest for review: narrative commentary
El Bashir, H., Laundy, M., Booy, R., Diagnosis and treatment of bacterial meningitis, Archives of Disease in Childhood, 88, 615-620, 2003	Study design not of interest for review: narrative commentary
Fitch, M. T., Abrahamian, F. M., Moran, G. J., Talan, D. A., Emergency department management of meningitis and encephalitis, Infectious Disease Clinics of North America, 22, 33-52, v-vi, 2008	Study design not of interest for review: narrative commentary
Glimaker, M., Johansson, B., Bell, M., Ericsson, M., Blackberg, J., Brink, M., Lindquist, L., Sjolin, J., Early lumbar puncture in adult bacterial meningitis--rationale for revised guidelines, Scandinavian Journal of Infectious DiseasesScand J Infect Dis, 45, 657-63, 2013	Study design not of interest for review: narrative commentary
Gopal, A. K., Whitehouse, J. D., Simel, D. L., Corey, G. R., Cranial computed tomography before lumbar puncture: A prospective clinical evaluation, Archives of Internal Medicine, 159, 2681-2685, 1999	Participants does not match protocol criteria: patients with meningitis was <50% of total participants included
Hasbun, R., Update and advances in community acquired bacterial meningitis, Current Opinion in	Study design not of interest for review: narrative

Study	Reason for Exclusion
Infectious DiseasesCurr Opin Infect Dis, 32, 233-238, 2019	commentary
Haslam, R. H., Role of computed tomography in the early management of bacterial meningitis, The Journal of pediatrics, 119, 157-9, 1991	Study design not of interest for review: narrative commentary
Heckenberg, S. G. B., De Gans, J., Brouwer, M. C., Weisfelt, M., Piet, J. R., Spanjaard, L., Van Der Ende, A., Van De Beek, D., Clinical features, outcome, and meningococcal genotype in 258 adults with meningococcal meningitis: A prospective cohort study, Medicine, 87, 185-192, 2008	No relevant comparative data reported
Heyderman, R. S., Lambert, H. P., O'Sullivan, I., Stuart, J. M., Taylor, B. L., Wall, R. A., Early management of suspected bacterial meningitis and meningococcal septicaemia in adults, Journal of infection, 46, 75-77, 2003	Study design not of interest for review: narrative commentary
Heyderman, R. S., Robb, S. A., Kendall, B. E., Levin, M., Does computed tomography have a role in the evaluation of complicated acute bacterial meningitis in childhood?, 34, 870-5, 1992	No comparison of interest: study did not provide data on CT versus no CT
Imtiaz, A., Toomath, R., Computed tomography head scans prior to lumbar punctures in suspected meningitis, Internal Medicine Journal, 49, 55-58, 2019	No comparative data presented for people who did not undergo CT.
Joffe, A. R., Lumbar puncture and brain herniation in acute bacterial meningitis: a review, Journal of Intensive Care MedicineJ Intensive Care Med, 22, 194-207, 2007	Study design not of interest: narrative review with no studies relevant to this review.
Kwong, K. L., Chiu, W. K., Potential risk of fatal cerebral herniation after lumbar puncture in suspected CNS infection, Hong Kong Journal of Paediatrics, 14, 22-28, 2009	Study design does not meet inclusion criteria: narrative review
McGill, F., Heyderman, R. S., Michael, B. D., Defres, S., Beeching, N. J., Borrow, R., Glennie, L., Gaillemin, O., Wyncoll, D., Kaczmarski, E., Nadel, S., Thwaites, G., Cohen, J., Davies, N. W., Miller, A., Rhodes, A., Read, R. C., Solomon, T., The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults, Journal of InfectionJ Infect, 72, 405-38, 2016	Publication type not relevant for this review: guideline
Mellor, D. H., The place of computed tomography and lumbar puncture in suspected bacterial meningitis, Archives of Disease in Childhood, 67, 1417-1419, 1992	Study design not of interest: narrative commentary.
Meyer, C. N., Augustesen, S., Models of predicting the risk of brain herniation in bacterial meningitis, Clinical Microbiology and Infection, 15, S335-S336, 2009	Conference Paper
Mirrakhimov, A. E., Gray, A., Ayach, T., When should brain imaging precede lumbar puncture in cases of suspected bacterial meningitis?, Cleveland Clinic journal of medicine, 84, 111-	Study design not of interest for review: narrative commentary

Study	Reason for Exclusion
113, 2017	
Nagra, I., Wee, B., Short, J., Banerjee, A. K., The role of cranial CT in the investigation of meningitis, JRSM Short ReportsJRSM Short Rep, 2, 20, 2011	No comparative data presented for people who did not have CT scans. No outcomes of interest presented.
Oliveira, C. R., Morriss, M. C., Mistrot, J. G., Cantey, J. B., Doern, C. D., Sánchez, P. J., Brain magnetic resonance imaging of infants with bacterial meningitis, 165, 134-9, 2014	No comparison of interest: study did not provide information on lumbar puncture
Ostergaard,C., Konradsen,H.B., Samuelsson,S., Clinical presentation and prognostic factors of Streptococcus pneumoniae meningitis according to the focus of infection, BMC Infectious Diseases, 5, 93-, 2005	Comparison not of interest for review: survivors vs non survivors
Park, N., Hasbun, R., Comparison of four recommendations guiding the use of neuroimaging in the management of bacterial meningitis, Open Forum Infectious Diseases, 6 (Supplement 2), S507, 2019	Conference abstract
Proulx, N., Frechette, D., Toye, B., Chan, J., Kravcik, S., Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis, QJM - Monthly Journal of the Association of Physicians, 98, 291-298, 2005	Comparison not of interest for review: survivors vs non survivors
Rennick, G., Shann, F., De Campo, J., Cerebral herniation during bacterial meningitis in children, British medical journal, 306, 953-955, 1993	No comparative data between neuroimaging prior to lumbar puncture versus no neuroimaging prior to lumbar puncture.
Riordan, F. A. I., Cant, A. J., When to do a lumbar puncture, Archives of disease in childhood, 87, 235-237, 2002	Study design not of interest: narrative commentary focussed on indications/contraindications for lumbar puncture
Salazar, L., Hasbun, R., Cranial Imaging Before Lumbar Puncture in Adults With Community-Acquired Meningitis: Clinical Utility and Adherence to the Infectious Diseases Society of America Guidelines, Clinical Infectious DiseasesClin Infect Dis, 64, 1657-1662, 2017	Comparison not of interest for review: in the CT not indicated arm, 87.3% of the population received CT
Schuh, S., Lindner, G., Exadaktylos, A. K., Muhlemann, K., Tauber, M. G., Determinants of timely management of acute bacterial meningitis in the ED, American journal of emergency medicine, 31, 1056-1061, 2013	No relevant comparison for review: study does not report outcomes for people who did or did not have neuroimaging
Stockdale, A. J., Weekes, M. P., Aliyu, S. H., An audit of acute bacterial meningitis in a large teaching hospital 2005-10, QjmQjm, 104, 1055-63, 2011	Study design not of interest for review: non-comparative study (audit)
Swanson, D., Meningitis, Pediatrics in Review, 36, 514-524, 2015	Study type not of interest for this review: commentary
Turner, T., Risk of cerebral herniation due to lumbar puncture in children with suspected meningitis, 28, 2003	No comparison of interest for this review
Wall, E. C., Chan, J. M., Gil, E., Heyderman, R. S., Acute bacterial meningitis, Current Opinion in Neurology, 26, 26, 2021	Study design not of interest for review: narrative commentary

Excluded economic studies

No economic evidence was identified for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What is the role of neuroimaging prior to lumbar puncture?

No research recommendation was made for this review.