National Institute for Health and Care Excellence

Guideline version (Consultation)

Subarachnoid haemorrhage

[H] Evidence review for managing hydrocephalus

NICE guideline <number>

Evidence review underpinning

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Evidence review underpinning recommendations 1.3.4 to 1.3.5 and research recommendations in the NICE guideline.

1.1 Review question: What is the clinical and cost effectiveness of options for managing hydrocephalus?

1.2 Introduction

Hydrocephalus occurs when excess cerebrospinal fluid (CSF) accumulates within the ventricular system of the brain. Hydrocephalus is usually associated with raised intracranial pressure.

Hydrocephalus is a common and potentially devastating complication of aneurysmal subarachnoid haemorrhage. Its incidence is approximately 20-30% and its onset can be acute (generally within 48 hours of ictus) or less commonly chronic after a delay of weeks or even months. Subarachnoid haemorrhage can cause hydrocephalus by obstructing CSF flow through the ventricular system or by compromising reabsorption of CSF through the arachnoid granulations.

Acute hydrocephalus presents with headache, nausea and vomiting, visual disturbance, drowsiness, coma or death. Chronic hydrocephalus will often present after an interval with a gradual neurological and functional deterioration, primarily affecting cognition, mobility, and sphincter control.

In current practice there are several different treatments for hydrocephalus, including temporary or permanent CSF diversion with serial lumbar puncture, external ventricular or lumbar drain, or ventriculo-peritoneal shunt. There is significant variation in practice between individual neurosurgeons and neurosurgical units with no accepted national standard.

1.3 PICO table

For full details see the review protocol in Appendix A:.

Table 1: PICO characteristics of review question

Population	Adults (16 and older) with a confirmed subarachnoid haemorrhage caused by a suspected or confirmed ruptured aneurysm with hydrocephalus. Strata: • Acute hydrocephalus (within acute admission / within 30 days of ictus) • Chronic hydrocephalus (post discharge / after 30 days from ictus)
Interventions	• Shunt surgery • External ventricular drain surgery • Lumbar puncture (serial) • Lumbar drain
Comparisons	• To each other • To no treatment
Outcomes	CRITICAL: • Mortality • Health and social-related quality of life (any validated measure) • Degree of disability or dependence in daily activities, (any validated measure e.g. Modified Rankin Scale and patient-reported outcome measures)

	IMPORTANT: • Risk of subsequent subarachnoid haemorrhage • Return to daily activity (e.g. driving, work) • Complications of procedure (including infection, Intracranial haemorrhage, epilepsy, cerebral infarction) • Repeat procedure
Study design	• Randomised controlled trials (RCTs), systematic reviews of RCTs. • If insufficient RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders (age), starting with prospective cohort studies.

1.4 Clinical evidence

1.4.1 Included studies

Two studies from 4 papers were included in the review;[6-8, 64] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

See also the study selection flow chart in Appendix C:, study evidence tables in Appendix D:, forest plots in Appendix E: and GRADE tables in Appendix G:.

1.4.2 Excluded studies

See the excluded studies list in Appendix J:.

1.4.3 1 Summary of clinical studies included in the evidence review

2 **Table 2: Summary of studies included in the evidence review**

Study	Intervention and comparison	Population	Outcomes	Comments
Chen 2009[6/7] /Chen 2014[8]	**Shunt surgery:** A treatment group underwent VPS operation. The programmable valve VPS system usually connected the right ventricle with the peritoneal space, with the aim of avoiding injury to the language centres on the left side of the brain. Shunts were usually equipped with reservoirs that were used for transiently increasing output and for testing the patency of flow. After shunt implantation the resumption of rehabilitation was usually prompt. Patients are typically observed for 2–3 days postoperatively, before returning to rehabilitation. N=35 **No additional treatment:** The control group did not undergo the operation, receiving standard rehabilitation only. N=16 Follow-up: 3 months	Chronic hydrocephalus Patients with disorders of consciousness following aSAH. All 51 subjects fulfilled the clinical criterion of presumed chronic normal pressure hydrocephalus. Mean age (SD): 59 years (13) China	• Degree of disability • Length of hospital stay	Results from trial reported in three papers as trial continued. Prospective cohort study. Matched control group. There were no significant differences between the 2 groups at baseline in terms of age, sex, time since aSAH, and admission GCS.
Yu 2016[64]	**Shunt surgery:** Underwent VPS surgery, whereby 18	Chronic hydrocephalus	• Degree of disability	Retrospective cohort study. Groups comparable for age.

Study	Intervention and comparison	Population	Outcomes	Comments
	received it in the right front and 10 received it in the left front. N=28 **No additional treatment:** Did not receive VPS. All patients underwent standardised rehabilitation procedure including physical, behavioural, and speech therapy. N=18 Following confirmation of aSAH, patients were taken to the operating room for haematoma evacuation or clipping of the aneurysm or decompressive craniotomy. An external ventricular drain (EVD) was placed in all patients with hydrocephalus or ventricular haemorrhage while clipping or coiling. Follow-up: 1 year	Poor grade (Hunt and Hess grade IV and V) aSAH patients with secondary normal pressure hydrocephalus. Mean age (SD): 57 (9) China		Control group elected not to receive VPS due to their own or family choice or because they could not afford treatment. All patients with acute hydrocephalus received EVD.

1 See Appendix D:for full evidence tables.

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1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Chronic Hydrocephalus – Shunt surgery versus no additional treatment

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Anticipated absolute effects	
			Risk with control	Risk difference with shunt surgery (95% CI)
Degree of disability - Consciousness (GCS) at 30 days Scale from: 3 to 15.	51 (1 study) 30 days	⨁⨁⨀⨀ LOW1 due to risk of bias	The mean degree of disability (GCS) at 30 days in the control groups was 6.5	The mean degree of disability (GCS) at 30 days in the intervention groups was 4.7 higher (3.2 to 6.2 higher)
Degree of disability - Consciousness (GCS) at 3 months Scale from: 3 to 15.	51 (1 study) 3 months	⨁⨁⨀⨀ LOW1 due to risk of bias	The mean degree of disability (GCS) at 3 months in the control groups was 6.56	The mean degree of disability (GCS) at 3 months in the intervention groups was 5.47 higher (3.72 to 7.22 higher)
Degree of disability (GOS) at 3 months Scale from: 1 to 5.	46 (1 study) 3 months	⨁⨀⨀⨀ VERY LOW12 due to risk of bias, imprecision	The mean degree of disability (GOS) at 3 months in the control groups was 2.72	The mean degree of disability (GOS) at 3 months in the intervention groups was 0.42 higher (0.04 lower to 0.88 higher)
Degree of disability (GOS) at 1 year Scale from: 1 to 5.	46 (1 study) 1 year	⨁⨁⨀⨀ LOW1 due to risk of bias	The mean degree of disability (GOS) at 1 year in the control groups was 2.83	The mean degree of disability (GOS) at 1 year in the intervention groups was 0.81 higher (0.36 to 1.26 higher)
Degree of disability (MMSE) at 30 days Scale from: 0 to 30.	39 (1 study) 30 days	⨁⨁⨀⨀ LOW1 due to risk of bias	The mean degree of disability (MMSE) at 30 days in the control groups was 18.6	The mean degree of disability (MMSE) at 30 days in the intervention groups was 3.7 higher (1.66 to 5.74 higher)
Degree of disability (MMSE) at 3-6 months Scale from: 0 to 30.	85 (2 studies) 3 to 6 months	⨁⨁⨀⨀ LOW1 due to risk of bias	The mean degree of disability (MMSE) at 3-6 months in the control groups was 14.46	The mean degree of disability (MMSE) at 3-6 months in the intervention groups was 9.16 higher (8.05 to 10.27 higher)
Degree of disability (MMSE) 1 year Scale from: 0 to 30.	46 (1 study) 1 year	⨁⨁⨀⨀ LOW1 due to risk of bias	The mean degree of disability (MMSE) 1 year in the control groups	The mean degree of disability (MMSE) 1 year in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Anticipated absolute effects	
			Risk with control	Risk difference with shunt surgery (95% CI)
			was 12.4	11.88 higher (10.56 to 13.2 higher)
Degree of disability (Barthel Index) at 30 days Scale from: 0 to 100.	39 (1 study) 30 days	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	The mean degree of disability (Barthel index) at 30 days in the control groups was 47	The mean degree of disability (Barthel index) at 30 days in the intervention groups was 10.3 higher (1.44 to 19.16 higher)
Degree of disability (Barthel Index) at 6 months Scale from: 0 to 100.	39 (1 study) 6 months	⨁⨁⊖⊖ LOW1 due to risk of bias	The mean degree of disability (Barthel index) at 6 months in the control groups was 46.3	The mean degree of disability (Barthel index) at 6 months in the intervention groups was 36 higher (26.54 to 45.46 higher)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias. 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs				

1 **Table 4: Evidence not suitable for GRADE analysis: Chronic Hydrocephalus – Shunt surgery versus no additional treatment**

Outcome	Study (no. of participants)	Risk of bias	Comparison results	Intervention results	*P* value
Length of hospital stay (days)	Chen 2014[8] (51)	Very high	Median: 3	Median: 2	<0.01

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3 See Appendix G: for full GRADE tables.

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1.5 Economic evidence

1.5.1 Included studies

No health economic studies were included.

1.5.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix H:.

1.5.3 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 5: UK costs of treatments for shunt surgery

Procedure	Description	Average cost
Ventriculoperitoneal shunt surgery	Very Major Intracranial Procedures, 19 years and over, with CC Score 12+; [NHS Reference Cost code: AA52A]	
	Non-elective	£13,579
	Elective	£13,292
Lumbar drain	Major intradural spinal procedures [NHS Reference Cost code: HC71Z]	
	Non-elective	£8,023
	Elective	£7,042

Source: NHS Reference Costs 2018/19[43]

1.6 Evidence statements

1.6.1 Clinical evidence statements

The outcome from 1 study was not suitable for inclusion in the GRADE summary tables. One study reported that the median length of stay was statistically significantly lower (2 days versus 3 days) in patients who received shunt surgery when compared to those who received no additional treatment. (n=51, high risk of bias).

1.6.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The outcomes that matter most

The committee considered the critical outcomes for decision making to be mortality, health and social-related quality of life and degree of disability (as measured by validated tools such as the modified Rankin scale or Glasgow outcome scale). Subsequent subarachnoid

haemorrhage, return to daily activity, complications of intervention and repeat procedures were important outcomes.

No evidence was identified for mortality, health and social-related quality of life, subsequent subarachnoid haemorrhage, return to daily activity, complications of intervention and repeat procedures.

1.7.2 The quality of the evidence

There was no evidence on the management of acute hydrocephalus.

In two cohort studies on the management of chronic hydrocephalus, the intervention and control groups were matched for the age, but there was no adjustment of outcome data for any confounders. The evidence from these studies was of low or very low quality, mostly due to the non-randomised design and high risk of selection bias, and a lack of adjustment for key confounding factors. Serious imprecision was also noted for some of the outcome data limiting the certainty of the observed results. The committee also highlighted possible heterogeneity within the population of one study, which reported that people in the control group elected not to have the intervention because they could not afford treatment. The committee considered that other confounding factors linked with socioeconomic status, may have affected people's health both before admission and at follow-up, biasing the outcomes recorded.

The committee noted that the population who received shunt surgery and the control group in the studies on managing chronic hydrocephalus appeared to have high levels of disability at presentation and at follow-up, and may not be reflective of a general aSAH population. This further reduced the committee's confidence in the evidence to inform any potential recommendation.

The committee recognised the low quality of available evidence on the management of chronic hydrocephalus, and particularly the absence of evidence in areas such as use of lumbar puncture that are used in clinical practice. They also noted that the management of chronic hydrocephalus can vary significantly between patients as it depends on the person's symptoms and the severity of their neurological deterioration, both of which could be highly variable. As such, the committee were unable to use the evidence available to support a recommendation, and instead made a consensus recommendation based on current clinical practice. The committee discussed making a research recommendation for chronic hydrocephalus but concluded that research in this area might not be feasible within a reasonable timeframe, nor impact clinical practice and was therefore not of high priority.

1.7.3 Benefits and harms

<u>Acute hydrocephalus</u>

No evidence was identified for the management of acute hydrocephalus.

The committee noted that acute hydrocephalus is a common and important complication of aneurysmal subarachnoid haemorrhage, which can cause serious harm or death. The committee agreed that these risks can be mitigated by drainage or diversion of cerebrospinal fluid (CSF), but acknowledged that any decision to intervene with invasive and potentially risky procedures such as lumbar puncture and ventricular drainage would depend on the speed and severity of any associated neurological deterioration. Although not identified from the evidence on managing hydrocephalus, the committee also noted from their clinical experience that there is a recognised risk with invasive interventions such as shunt surgery, external ventricular drain surgery and lumbar drain, which include infection, epilepsy, cerebral infarction, or intracranial haemorrhage. The committee discussed that in their experience CSF drainage or diversion is a potentially useful intervention but in individual patients the risks and benefits need careful judgement. The committee agreed to make a

consensus recommendation to consider drainage or diversion of cerebrospinal fluid in people with aSAH and acute hydrocephalus but were unable to develop recommendations for a preferred technique.

The lack of evidence for the clinical and cost effectiveness of the interventions for acute hydrocephalus and the committee's knowledge of potential risks of treatments contributed to the committee's decision to make a weak recommendation.

As no evidence was found for the management of acute hydrocephalus the committee made a research recommendation to evaluate the most effective method of cerebrospinal fluid drainage or diversion for symptomatic acute hydrocephalus.

Chronic hydrocephalus

The committee noted evidence from 4 papers from 2 non-randomised studies comparing shunt surgery to no additional treatment to treat chronic normal pressure hydrocephalus in people with aneurysmal subarachnoid haemorrhage. The committee agreed that there was a trend towards benefit with shunt surgery with a reduced degree of disability at follow-up up to 1 year following intervention. However, the committee considered that the quality and quantity of evidence was too low to draw any conclusions or support recommendations.

The committee discussed that chronic hydrocephalus in people with subarachnoid haemorrhage is an uncommon condition but can develop several weeks or months after the ictus with gradual neurological and functional deterioration. The committee agreed that in current practice the management of chronic hydrocephalus depends on the symptomatology of the patient, but in patients with progressive neurological deterioration CSF drainage will improve symptoms in the majority of patients. The committee also acknowledged that there may be uncertainty about the anticipated benefits of CSF drainage in some patients with chronic hydrocephalus, and in these cases the impact on symptoms of draining a small volume of CSF via a lumbar puncture can sometimes support decisions about a more definitive procedure. On the basis of this discussion, the committee made a consensus recommendation to consider drainage or diversion of cerebrospinal fluid for people with persisting and/or progressive symptoms and a clinical diagnosis of chronic hydrocephalus. The committee added that where there is uncertainty about any anticipated therapeutic benefit of intervention, a trial of temporary CSF drainage to guide the need for permanent CSF diversion could be considered.

1.7.4 Cost effectiveness and resource use

No published economic evaluations were identified for this review. Therefore, unit costs were presented to the committee for consideration of cost effectiveness.

The committee acknowledged that interventions for managing acute hydrocephalus are costly but recognised that conservative management of acute hydrocephalus is associated with severe disability or death. The committee therefore made a consensus recommendation to consider CSF drainage or diversion in people with acute hydrocephalus, which reflects current practice and is not expected to have a significant resource impact for the NHS.

The committee noted that in current clinical practice people with persistent or progressive symptoms due to chronic hydrocephalus would be considered for drainage or diversion of cerebrospinal fluid, even though there may be uncertainty about the therapeutic benefit of intervention. The committee also discussed the high costs of permanent CSF diversion (£13,292 - £13-579 for ventriculo-peritoneal shunt; £7,042 - £8,023 for lumbar drain), and agreed that if there is uncertainty about the anticipated therapeutic benefit of treatment, short-term CSF drainage via a lumbar puncture may guide the need for permanent CSF diversion.

The recommendations made by the committee are reflective of UK current practice and therefore will not have a substantial resource impact.

1.7.5 Other factors the committee took into account

The committee agreed that good practice for the diagnosis and management of hydrocephalus includes providing clear information for patients and their families/carers and involving them in decision-making.

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1 Appendices

2 Appendix A: Review protocols

3 **Table 6: Review protocol: Managing hydrocephalus**

ID	Field	Content
0.	PROSPERO registration number	CRD42019146751
1.	Review title	What is the clinical and cost effectiveness of options for managing hydrocephalus?
2.	Review question	What is the clinical and cost effectiveness of options for managing hydrocephalus?
3.	Objective	To determine which intervention to manage hydrocephalus is the most clinically and cost-effective. Hydrocephalus is recognised as a serious complication of aneurysmal subarachnoid haemorrhage associated with increased morbidity.
4.	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: • English language only The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Aneurysmal subarachnoid haemorrhage
6.	Population	Inclusion: Adults (16 and older) with a confirmed subarachnoid haemorrhage caused by a suspected or confirmed ruptured aneurysm with hydrocephalus. Exclusion: • Adults with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger.
7.	Intervention/Exposure/Test	• Shunt surgery • External ventricular drain surgery • Lumbar puncture (serial)

		• Lumbar drain
8.	Comparator/Reference standard/Confounding factors	Comparators: • To each other • To no treatment
9.	Types of study to be included	• Randomised controlled trials (RCTs), systematic reviews of RCTs. • If insufficient RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders (age), starting with prospective cohort studies.
10.	Other exclusion criteria	Exclusions: • Non- English language studies • Abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	
12.	Primary outcomes (critical outcomes)	• Mortality • Health and social-related quality of life (any validated measure) • Degree of disability or dependence in daily activities, (any validated measure e.g. Modified Rankin Scale and patient-reported outcome measures)
13.	Secondary outcomes (important outcomes)	• Risk of subsequent subarachnoid haemorrhage • Return to work (driving) • Complications of procedure (including infection, Intracranial haemorrhage, epilepsy, cerebral infarction) • Repeat procedure Short term outcomes <30 days will be grouped. Outcomes will be reported monthly for the first year and grouped at yearly time-points thereafter.
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. EviBASE will be used for data extraction. If not an intervention review, add: A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).

15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) • Non randomised study, including cohort studies: Cochrane ROBINS-I 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. • The risk of bias across all available evidence was 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/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • Subgroups will be investigated separately if meta-analysed results show heterogeneity.
17.	Analysis of sub-groups	Strata: • Acute hydrocephalus (within acute admission / within 30 days of ictus) • Chronic hydrocephalus (post discharge / after 30 days from ictus) Subgroups: • n/a

<table>
<tr><td rowspan="8">18.</td><td rowspan="8">Type and method of review</td><td>☒</td><td colspan="3">Intervention</td></tr>
<tr><td>☐</td><td colspan="3">Diagnostic</td></tr>
<tr><td>☐</td><td colspan="3">Prognostic</td></tr>
<tr><td>☐</td><td colspan="3">Qualitative</td></tr>
<tr><td>☐</td><td colspan="3">Epidemiologic</td></tr>
<tr><td>☐</td><td colspan="3">Service Delivery</td></tr>
<tr><td>☐</td><td colspan="3">Other (please specify)</td></tr>
<tr><td></td><td colspan="4"></td></tr>
<tr><td>19.</td><td>Language</td><td colspan="4">English</td></tr>
<tr><td>20.</td><td>Country</td><td colspan="4">England</td></tr>
<tr><td>21.</td><td>Anticipated or actual start date</td><td colspan="4"></td></tr>
<tr><td>22.</td><td>Anticipated completion date</td><td colspan="4">3 February 2021</td></tr>
<tr><td rowspan="8">23.</td><td rowspan="8">Stage of review at time of this submission</td><td colspan="2">Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td colspan="2">Preliminary searches</td><td>☑</td><td>☑</td></tr>
<tr><td colspan="2">Piloting of the study selection process</td><td>☑</td><td>☑</td></tr>
<tr><td colspan="2">Formal screening of search results against eligibility criteria</td><td>☑</td><td>☑</td></tr>
<tr><td colspan="2">Data extraction</td><td>☑</td><td>☑</td></tr>
<tr><td colspan="2">Risk of bias (quality) assessment</td><td>☑</td><td>☑</td></tr>
<tr><td colspan="2">Data analysis</td><td>☑</td><td>☑</td></tr>
<tr><td></td><td colspan="4"></td></tr>
<tr><td>24.</td><td>Named contact</td><td colspan="4">5a. Named contact
National Guideline Centre

5b Named contact e-mail
SAH@nice.org.uk

5e Organisational affiliation of the review
National Institute for Health and Care Excellence (NICE) and the National Guideline Centre</td></tr>
<tr><td>25.</td><td>Review team members</td><td colspan="4">From the National Guideline Centre:
• Ms Gill Ritchie
• Mr Ben Mayer
• Mr Audrius Stonkus
• Mr Vimal Bedia
• Ms Emma Cowles</td></tr>
</table>

		• Ms Jill Cobb • Ms Amelia Unsworth	
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.	
27.	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.	
28.	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.	
29.	Other registration details		
30.	Reference/URL for published protocol		
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Subarachnoid haemorrhage; hydrocephalus	
33.	Details of existing review of same topic by same authors	None	
34.	Current review status	☐	Ongoing
		☐	Completed but not published
		☐	Completed and published

		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information		
36.	Details of final publication	www.nice.org.uk	

1
2

1 **Table 7: Health economic review protocol**

Review question	All questions where health economic evidence applicable
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual.[41] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will decide based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded based on applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland).

	• Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

1

Appendix B: Literature search strategies

This literature search strategy was used for the following review;

- What is the clinical and cost effectiveness of options for managing hydrocephalus?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[41]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 24 June 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 24 June 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 6 of 12 CENTRAL to 2020 Issue 6 of 12	None

Medline (Ovid) search terms

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/

12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
27.	25 not 26
28.	limit 27 to English language
29.	exp "Sensitivity and Specificity"/
30.	(sensitivity or specificity).ti,ab.
31.	((pre test or pretest or post test) adj probability).ti,ab.
32.	(predictive value* or PPV or NPV).ti,ab.
33.	likelihood ratio*.ti,ab.
34.	likelihood function/
35.	((area under adj4 curve) or AUC).ti,ab.
36.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
37.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
38.	gold standard.ab.
39.	or/29-38
40.	Epidemiologic studies/
41.	Observational study/
42.	exp Cohort studies/
43.	(cohort adj (study or studies or analys* or data)).ti,ab.
44.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
45.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
46.	Controlled Before-After Studies/
47.	Historically Controlled Study/
48.	Interrupted Time Series Analysis/
49.	(before adj2 after adj2 (study or studies or data)).ti,ab.
50.	exp case control study/
51.	case control*.ti,ab.
52.	Cross-sectional studies/
53.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.

54.	or/40-53
55.	Meta-Analysis/
56.	exp Meta-Analysis as Topic/
57.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
58.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
59.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
60.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
61.	(search* adj4 literature).ab.
62.	(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.
63.	cochrane.jw.
64.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
65.	or/55-64
66.	randomized controlled trial.pt.
67.	controlled clinical trial.pt.
68.	randomi#ed.ti,ab.
69.	placebo.ab.
70.	randomly.ti,ab.
71.	Clinical Trials as topic.sh.
72.	trial.ti.
73.	or/66-72
74.	28 and (39 or 54 or 65 or 73)
75.	hydrocephalus/ or hydrocephalus, normal pressure/
76.	(hydrocephalus or hydrocephaly).ti,ab.
77.	water on the brain.ti,ab.
78.	or/75-77
79.	74 and 78

1 **Embase (Ovid) search terms**

1.	*subarachnoid hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	Case report/ or Case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.

14.	12 not 13
15.	animal/ not human/
16.	Nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental animal/
19.	Animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
25.	23 not 24
26.	limit 25 to English language
27.	exp "sensitivity and specificity"/
28.	(sensitivity or specificity).ti,ab.
29.	((pre test or pretest or post test) adj probability).ti,ab.
30.	(predictive value* or PPV or NPV).ti,ab.
31.	likelihood ratio*.ti,ab.
32.	((area under adj4 curve) or AUC).ti,ab.
33.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
34.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
35.	diagnostic accuracy/
36.	diagnostic test accuracy study/
37.	gold standard.ab.
38.	or/27-37
39.	Clinical study/
40.	Observational study/
41.	family study/
42.	longitudinal study/
43.	retrospective study/
44.	prospective study/
45.	cohort analysis/
46.	follow-up/
47.	cohort*.ti,ab.
48.	46 and 47
49.	(cohort adj (study or studies or analys* or data)).ti,ab.
50.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
51.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
52.	(before adj2 after adj2 (study or studies or data)).ti,ab.
53.	exp case control study/
54.	case control*.ti,ab.
55.	cross-sectional study/
56.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.

57.	or/39-45,48-56
58.	random*.ti,ab.
59.	factorial*.ti,ab.
60.	(crossover* or cross over*).ti,ab.
61.	((doubl* or singl*) adj blind*).ti,ab.
62.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
63.	crossover procedure/
64.	single blind procedure/
65.	randomized controlled trial/
66.	double blind procedure/
67.	or/58-66
68.	systematic review/
69.	meta-analysis/
70.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
71.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
72.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
73.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
74.	(search* adj4 literature).ab.
75.	(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.
76.	cochrane.jw.
77.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
78.	or/68-77
79.	26 and (38 or 57 or 67 or 78)
80.	normotensive hydrocephalus/ or hydrocephalus/
81.	(hydrocephalus or hydrocephaly).ti,ab.
82.	water on the brain.ti,ab.
83.	or/80-82
84.	79 and 83

1 **Cochrane Library (Wiley) search terms**

#1.	MeSH descriptor: [Subarachnoid Hemorrhage] explode all trees
#2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) near/3 (hemorrhag* or haemorrhag* or bleed* or blood*)):ti,ab
#3.	(SAH or aSAH):ti,ab
#4.	MeSH descriptor: [Intracranial Aneurysm] explode all trees
#5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) near/3 (aneurysm* or aneurism* or hematoma* or haematoma*)):ti,ab
#6.	(OR #1-#5)
#7.	MeSH descriptor: [Hydrocephalus] explode all trees
#8.	(hydrocephalus or hydrocephaly):ti,ab
#9.	water on the brain.ti,ab
#10.	(or #7-#9)
#11.	#6 and #10

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to subarachnoid haemorrhage population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase.

Table 9: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2003 – 23 June 2020	Exclusions Health economics studies
Embase	2003 – 23 June 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 23 June 2020 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23

25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	26 and 43

1 **Embase (Ovid) search terms**

1.	subarachnoid hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/

21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

1 **NHS EED and HTA (CRD) search terms**

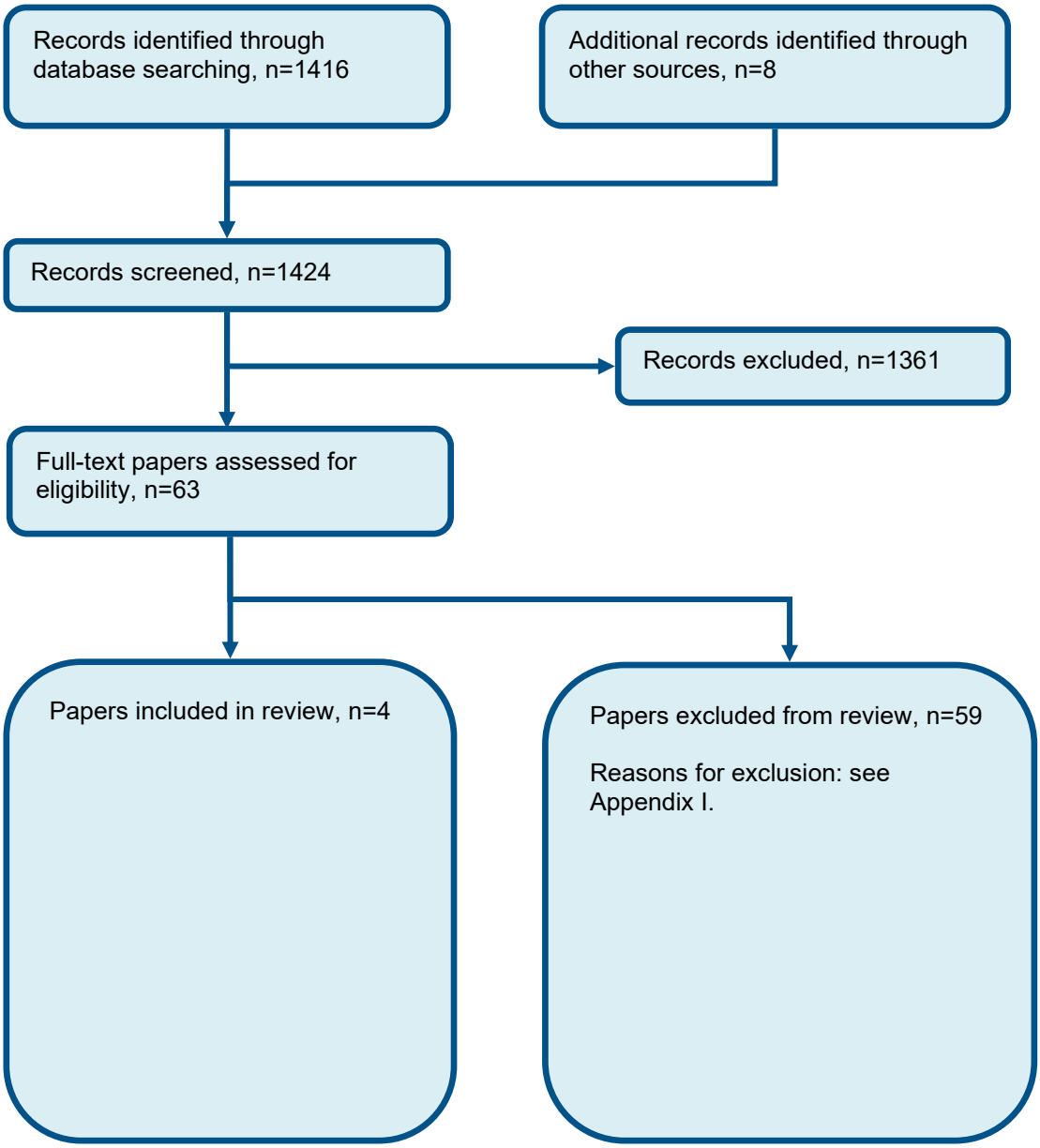
#1.	MeSH DESCRIPTOR Subarachnoid Hemorrhage EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES
#3.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)))
#4.	((SAH or aSAH))
#5.	#1 OR #2 OR #3 OR #4
#6.	MeSH DESCRIPTOR Aneurysm EXPLODE ALL TREES
#7.	((aneurysm* or hematoma* or haematoma*))
#8.	#6 OR #7
#9.	MeSH DESCRIPTOR Intracranial Aneurysm EXPLODE ALL TREES
#10.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (aneurysm* or hematoma* or haematoma*)))
#11.	#9 OR #10
#12.	MeSH DESCRIPTOR Aneurysm, ruptured
#13.	(((ruptur* or weak* or brain or trauma*) adj3 (aneurysm* or hematoma* or haematoma*)))
#14.	#12 OR #13
#15.	(#5 or #8 or #11 or #14)

2

3

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of managing hydrocephalus



Appendix D: Clinical evidence tables

Study	Chen 2014[8] (Chen 2009[7] / Chen 2009[6])
Study type	Prospective cohort study
Number of studies (number of participants)	1 (n=51)
Countries and setting	Conducted in China; Setting: Departments of Rehabilitation Medicine and Neurosurgery, Xuanwu Hospital, Capital Medical University, Beijing.
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Chronic hydrocephalus (post discharge / after 30 days from ictus)
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with disorders of consciousness following aSAH. All 51 subjects fulfilled the clinical criterion of presumed chronic normal pressure hydrocephalus.
Exclusion criteria	non-aSAH, such as trauma, arteriovenous malformation rupture, vasculitis; and (ii) pre-existing neurological disease. Twenty-seven patients were excluded due to the presence of other diseases, high-pressure hydrocephalus, or missed follow-up.
Recruitment/selection of patients	Consecutive series of patients included.
Age, gender and ethnicity	Age - Mean (SD): 59 (13). Gender (M:F): 23/28. Ethnicity: Not reported
Further population details	
Extra comments	Clinical diagnosis of hydrocephalus was based on the following characteristics: diagnosis of CNPH by an experienced neuroradiologist, who reviewed the CT scan images and calculated the width of the third ventricle (III) and CMI (B/A, where A is the largest width of the outer layer of the skull and B is the width of the lateral ventricles in the same layer).. Matched control group. There were no significant differences between the 2 groups at baseline in terms of age, sex, time since aSAH, and admission GCS.

	Consideration for confounding factors: Matched control group. There were no significant differences between the 2 groups at baseline in terms of age, sex, time since aSAH, and admission GCS.
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Shunt surgery. The programmable valve VPS system usually connects the right ventricle with the peritoneal space, with the aim of avoiding injury to the language centres on the left side of the brain. Shunts are usually equipped with reservoirs that are used for transiently increasing output and for testing the patency of flow. After shunt implantation the resumption of rehabilitation is usually prompt. Patients are typically observed for 2–3 days postoperatively, before returning to rehabilitation. Duration n/a. Concurrent medication/care: Lumbar puncture was used to measure ventricular pressure to distinguish normal or high-pressure hydrocephalus and to help in selecting the pressure of the shunt used for VPS. Computed tomography (CT) scans were used to investigate the patients' brain injuries when they were transferred to rehabilitation, and every 2–4 weeks during rehabilitation treatment. Indirectness: No indirectness (n=16) Intervention 2: No treatment. Received no shunt surgery. Duration n/a. Concurrent medication/care: Lumbar puncture was used to measure ventricular pressure to distinguish normal or high-pressure hydrocephalus and to help in selecting the pressure of the shunt used for VPS. Computed tomography (CT) scans were used to investigate the patients' brain injuries when they were transferred to rehabilitation, and every 2–4 weeks during rehabilitation treatment. Indirectness: No indirectness
Funding	Academic or government funding (National Natural Science Foundation of China (grant numbers 81171024 and 30770714), the Natural Science Foundation of Beijing (grant number 7102075) and the Ministry of Organization of the Beijing government (grant number 20071D0501800243).)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SHUNT SURGERY versus NO TREATMENT

Protocol outcome 1: Degree of disability or dependence in daily activities, (e.g. Modified Rankin Scale and patient-reported outcome measures)
- Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Glasgow Coma Scale at 30 days; Group 1: mean 11.2 (SD 3.4); n=35, Group 2: mean 6.5 (SD 2.03); n=16; Glasgow Coma Scale 0-15 Top=High is good outcome

Risk of bias: All domain – Very High, Selection - High, Confounding – High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: VPS: 59.94 years (11.88), Control: 58.19 years (16.45), p=0.67; Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Glasgow Coma Scale at 3 months; Group 1: mean 12.03 (SD 3.87); n=35, Group 2: mean 6.56 (SD 2.42); n=16; Glasgow Coma Scale 0-15 Top=High is poor outcome

Risk of bias: All domain – Very High, Selection - High, Confounding – High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: VPS: 59.94 years (11.88), Control: 58.19 years (16.45), p=0.67; Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Glasgow Outcome Scale at 3 months; Group 1: median 3; n=35, Group 2: median 2; n=16; Glasgow Outcome Scale 1-5 Top=High is good outcome, p<0.01 - Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): MMSE at 30 days; Group 1: mean 22.3 (SD 3.9); n=24, Group 2: mean 18.6 (SD 2.6); n=15; Mini Mental State Examination 0-30 Top=High is good outcome Risk of bias: All domain – Very High, Selection - High, Confounding – High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: VPS: 59.94 years (11.88), Control: 58.19 years (16.45), p=0.67; Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): MMSE at 6 months; Group 1: mean 26.4 (SD 2.4); n=24, Group 2: mean 18.5 (SD 2.9); n=15; Mini Mental State Examination 0-30 Top=High is good outcome Risk of bias: All domain – Very High, Selection - High, Confounding – High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: VPS: 59.94 years (11.88), Control: 58.19 years (16.45), p=0.67; Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Barthel Index at 30 days; Group 1: mean 57.3 (SD 15.5); n=24, Group 2: mean 47 (SD 12.5); n=15; Barthel Index 0-100 Top=High is good outcome Risk of bias: All domain – Very High, Selection - High, Confounding – High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: VPS: 59.94 years (11.88), Control: 58.19 years (16.45), p=0.67; Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Barthel Index at 6 months days; Group 1: mean 82.3 (SD 17); n=24, Group 2: mean 46.3 (SD 13); n=15; Barthel Index 0-100 Top=High is good outcome Risk of bias: All domain – Very High, Selection - High, Confounding – High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: VPS: 59.94 years (11.88), Control: 58.19 years (16.45), p=0.67; Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Mortality ; Health and social quality of life ; Subsequent subarachnoid haemorrhage ; Return to daily activity (e.g. work) ; Complications of procedure (infection, ICH, epilepsy, cerebral infarction) ; Repeat procedure

Study	Yu 2016[64]
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=46)
Countries and setting	Conducted in China; Setting: Hospital based
Line of therapy	Unclear
Duration of study	Intervention + follow up: 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Chronic hydrocephalus (post discharge / after 30 days from ictus)
Subgroup analysis within study	Not applicable
Inclusion criteria	Poor grade (Hunt and Hess grade IV and V) aSAH patients with secondary normal pressure hydrocephalus.
Exclusion criteria	Died within 2 weeks of hospitalisation, pre-existing neurological deficit, refused treatment or changed their address.
Recruitment/selection of patients	Retrospective selection of consecutive patients.
Age, gender and ethnicity	Age - Mean (SD): 57 (9). Gender (M:F): 26/20. Ethnicity: Not reported
Further population details	
Extra comments	Consideration for confounding factors: Groups comparable for age; no significant difference between the mean ages of the intervention and control groups
Indirectness of population	No indirectness
Interventions	(n=28) Intervention 1: Shunt surgery. The decision to perform VPS in poor grade patients was based on their clinical presentation and neurological imaging: normal lumbar CSF pressure (>180mmHg H2O excluded) with or without gait ataxia, cognitive disturbance and urinary incontinence, with distensible ventricles, no improvement in clinical function or deterioration with distensible ventricles, or no shrinkage of ventricles after drainage of CSF for 1 week. Underwent VPS surgery, whereby 18 received it in the right front and 10 received it in the left front. Duration n/a. Concurrent medication/care: When CT confirmed aSAH with mass effect the patient was taken to the operating room for hematoma evacuation and clipping of the aneurysm or decompressive craniotomy. The remaining patients were treated by endovascular occlusion. An external ventricular drain was placed in those patients with acute hydrocephalus during surgery. All patients received nimodipine, Mannitol, and hypervolemic, hypertensive and haemodilution therapy. Indirectness: No indirectness (n=18) Intervention 2: No treatment. Opted not to undergo VPS due to their own or family member choice or because

	they could not afford the cost of VPS management. . Duration n/a. Concurrent medication/care: When CT confirmed aSAH with mass effect the patient was taken to the operating room for hematoma evacuation and clipping of the aneurysm or decompressive craniotomy. The remaining patients were treated by endovascular occlusion. An external ventricular drain was placed in those patients with acute hydrocephalus during surgery. All patients received nimodipine, Mannitol, and hypervolemic, hypertensive and haemodilution therapy. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SHUNT SURGERY versus NO TREATMENT

Protocol outcome 1: Degree of disability or dependence in daily activities, (e.g. Modified Rankin Scale and patient-reported outcome measures)
- Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Glasgow Outcome Scale at 3 months; Group 1: mean 3.14 (SD 0.93); n=28, Group 2: mean 2.72 (SD 0.67); n=18; Glasgow Outcome Scale 1-5 Top=High is good outcome
Risk of bias: All domain – Very high, Selection - High, Confounding – High; Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Age (SD): VPS 55.7 years (9.4), Control 58.2 (8.8); Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Glasgow Outcome Scale at 1 year; Group 1: mean 3.64 (SD 1.03); n=28, Group 2: mean 2.83 (SD 0.51); n=18; Glasgow Outcome Scale 1-5 Top=High is good outcome
Risk of bias: All domain – Very high, Selection - High, Confounding – High; Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Age (SD): VPS 55.7 years (9.4), Control 58.2 (8.8); Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Mini Mental State Examination at 3 months; Group 1: mean 21.11 (SD 3.12); n=28, Group 2: mean 11.1 (SD 1.85); n=18; MMSE 0-30 Top=High is good outcome
Risk of bias: All domain – Very high, Selection - High, Confounding – High; Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Age (SD): VPS 55.7 years (9.4), Control 58.2 (8.8); Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Chronic hydrocephalus (post discharge / after 30 days from ictus): Mini Mental State Examination at 1 year; Group 1: mean 24.28 (SD 2.68); n=28, Group 2: mean 12.4 (SD 1.87); n=18; MMSE 0-30 Top=High is good outcome
Risk of bias: All domain – Very high, Selection - High, Confounding – High; Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Age (SD): VPS 55.7 years (9.4), Control 58.2 (8.8); Key confounders: Age; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Mortality ; Health and social quality of life ; Subsequent subarachnoid haemorrhage ; Return to daily activity (e.g. work) ; Complications of procedure (infection, ICH, epilepsy, cerebral infarction) ; Repeat procedure

1

Appendix E: Forest plots

E.1 Chronic Hydrocephalus – Shunt surgery versus no additional treatment

Figure 2: Degree of disability - Consciousness (GCS) at 30 days. Scale from: 3 to 15, high score represents a positive outcome.

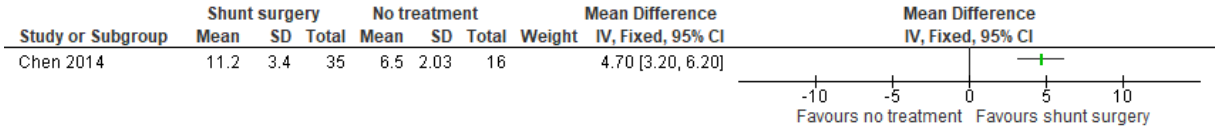


Figure 3: Degree of disability - Consciousness (GCS) at 3 months. Scale from: 3 to 15, high score represents a positive outcome.

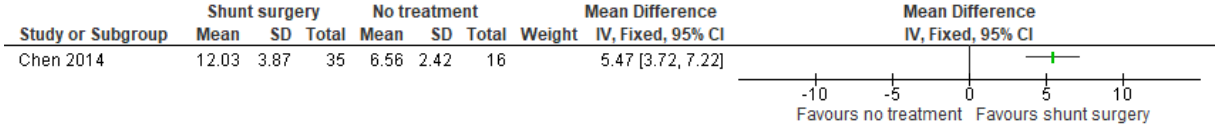


Figure 4: Degree of disability (GOS) at 3 months. Scale from: 1 to 5, high score represents a positive outcome.

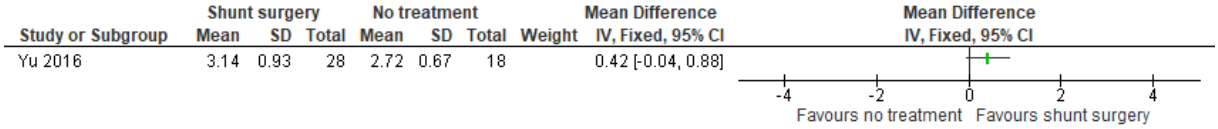


Figure 5: Degree of disability (GOS) at 1 year. Scale from: 1 to 5, high score represents a positive outcome.

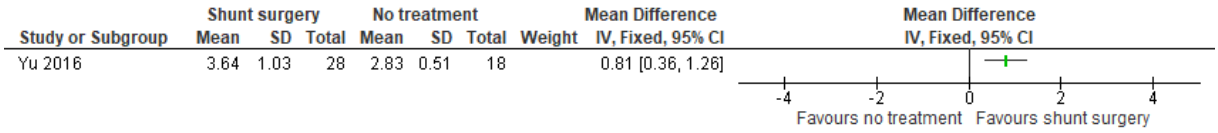


Figure 6: Degree of disability (MMSE) at 30 days. Scale from: 0 to 30, high score represents a positive outcome.

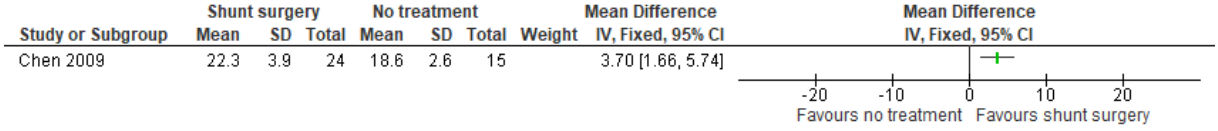


Figure 7: Degree of disability (MMSE) at 3 to 6 months. Scale from: 0 to 30, high score represents a positive outcome.

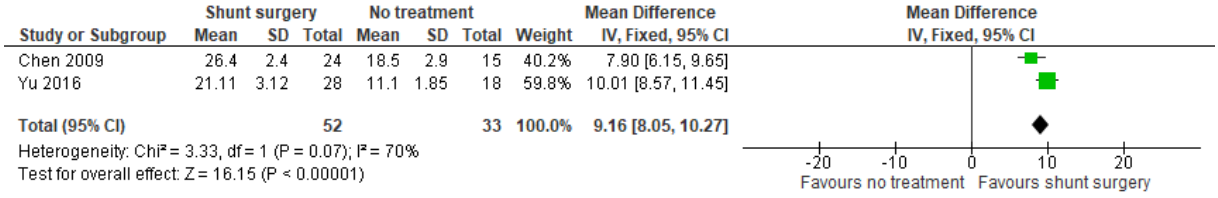


Figure 8: Degree of disability (MMSE) at 1 year. Scale from: 0 to 30, high score represents a positive outcome.

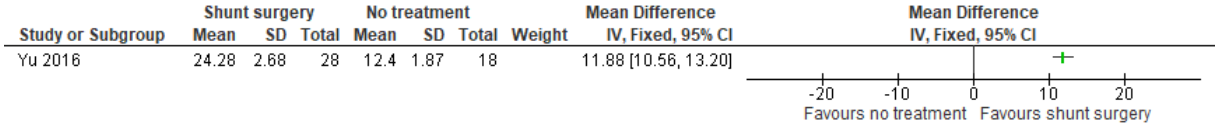


Figure 9: Degree of disability (Barthel Index) at 30 days. Scale from: 0 to 100, high score represents a positive outcome.

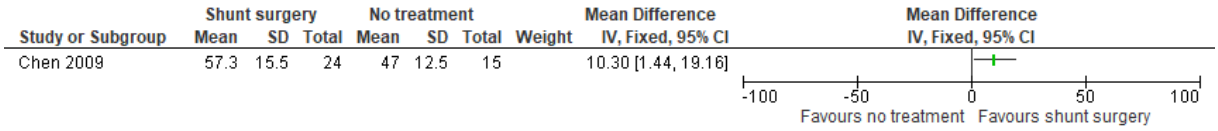
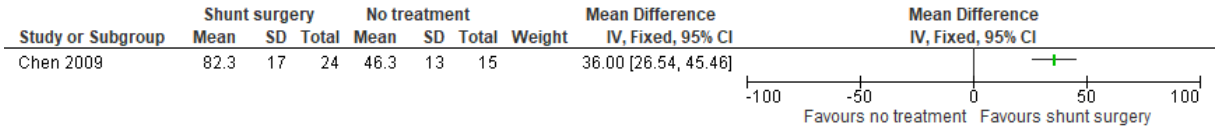


Figure 10: Degree of disability (Barthel Index) at 6 months. Scale from: 0 to 100, high score represents a positive outcome.



Appendix F: Minimal Important Difference for continuous outcomes

Table 10: Minimal important differences: Shunt surgery versus no treatment

Outcomes	Minimally important difference (MID)
Degree of disability (GOS) at 3 months	1.01
Degree of disability (GOS) at 1 year	1.21
Degree of disability (GCS) at 30 days	0.33
Degree of disability (GCS) at 3 months	0.25
Degree of disability (MMSE) at 30 days	2.3
Degree of disability (MMSE) at 3-6 months	2.38
Degree of disability (MMSE) 1 year	0.94
Degree of disability (Barthel Index) at 30 days	6.25
Degree of disability (Barthel Index) at 6 months	6.5

1 Appendix G: GRADE tables

2 **Table 11: Clinical evidence profile: Chronic Hydrocephalus – Shunt surgery versus no additional treatment**

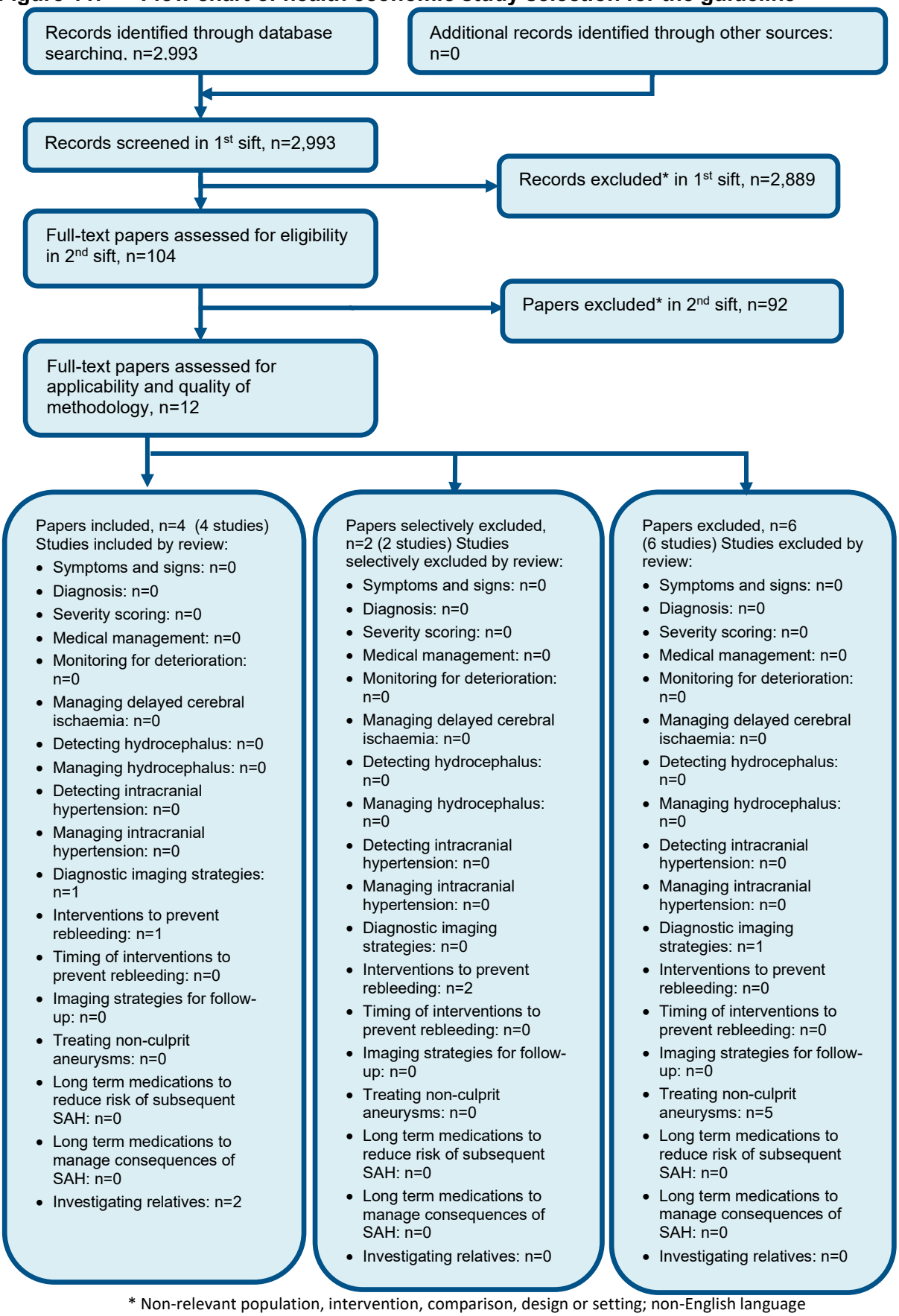
Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Chronic hydrocephalus: Shunt surgery versus no treatment	Control	Relative (95% CI)	Absolute		
Degree of disability – consciousness (GCS) at 30 days (follow-up 30 days; range of scores: 3-15; Better indicated by higher values)												
1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	16	-	MD 4.7 higher (3.2 to 6.2 higher)	⊕⊕OO LOW	CRITICAL
Degree of disability – consciousness (GCS) at 3 months (follow-up 3 months; range of scores: 3-15; Better indicated by higher values)												
1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	16	-	MD 5.47 higher (3.72 to 7.22 higher)	⊕⊕OO LOW	CRITICAL
Degree of disability (GOS) at 3 months (follow-up 3 months; range of scores: 1-5; Better indicated by higher values)												
1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	serious[2]	none	28	18	-	MD 0.42 higher (0.04 lower to 0.88 higher)	⊕OOO VERY LOW	CRITICAL
Degree of disability (GOS) at 1 year (follow-up 1 years; range of scores: 1-5; Better indicated by higher values)												
1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	28	18	-	MD 0.81 higher (0.36 to 1.26 higher)	⊕⊕OO LOW	CRITICAL
Degree of disability (MMSE) at 30 days (follow-up 30 days; range of scores: 0-30; Better indicated by higher values)												

1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	24	15	-	MD 3.7 higher (1.66 to 5.74 higher)	⊕⊕OO LOW	CRITICAL
Degree of disability (MMSE) at 3-6 months (follow-up 3 to 6 months; range of scores: 0-30; Better indicated by higher values)												
2	randomised trials	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	52	33	-	MD 9.16 higher (8.05 to 10.27 higher)	⊕⊕OO LOW	CRITICAL
Degree of disability (MMSE) 1 year (follow-up 1 years; range of scores: 0-30; Better indicated by higher values)												
1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	28	18	-	MD 11.88 higher (10.56 to 13.2 higher)	⊕⊕OO LOW	CRITICAL
Degree of disability (Bachel index) at 30 days (follow-up 30 days; range of scores: 0-100; Better indicated by higher values)												
1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	15	-	MD 10.3 higher (1.44 to 19.16 higher)	⊕OOO VERY LOW	CRITICAL
Degree of disability (Bachel index) at 6 months (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	observational studies	very serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	24	15	-	MD 36 higher (26.54 to 45.46 higher)	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Appendix H: Health economic evidence selection

Figure 11: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

1

1 Appendix I: Health economic evidence tables

2 None.

Appendix J: Excluded studies

J.1 Excluded clinical studies

Table 12: Studies excluded from the clinical review

Reference	Reason for exclusion
Al-Tamimi 2012[1]	Inappropriate population – prophylactic treatment
Boonyawanakij 2016[2]	Inappropriate population – non hydrocephalus
Borgmann 1990[3]	Inappropriate comparison – comparison of normal CSF levels
Capion 2019[4]	Inappropriate comparison – fast compared to slow closure of EVD
Carrau 2005[5]	Inappropriate study design – non comparative
Dey 2012[9]	Inappropriate study design – non comparative
Fang 2020[10]	Inappropriate population – non hydrocephalus
Fugate 2012[11]	Inappropriate study design – case report
Germanwala 2010[12]	Inappropriate study design – narrative report
Governale 2008[13]	Inappropriate population – non SAH hydrocephalus
Guresir 2009[14]	Inappropriate study design – non comparative
Hanggi 2008[15]	Inappropriate population – non hydrocephalus
Hasan 1989[16]	Inappropriate study design – non comparative (no adjustment)
Hayek 2017[17]	Inappropriate comparison – volume of CSF
Hoekema 2007[18]	Inappropriate study design – non comparative
Honeybul 2013[19]	Inappropriate study design - literature review
Jabbarli 2019[20]	Inappropriate population – non hydrocephalus
Jehan 2017[21]	Inappropriate population – Traumatic brain injury
Kang 2000[23]	Inappropriate comparison – techniques of shunting
Kang 2010[22]	Inappropriate comparison – distribution of IVH
Kasuya 1991[24]	Inappropriate population – prophylactic treatment
Kim 2018[25]	Inappropriate comparison – perimesencephalic SAH
Klimo 2004[26]	Inappropriate population – non hydrocephalus
Kwon 2008[27]	Inappropriate study design – predictive factors of hydrocephalus
Kwon 2008[28]	Inappropriate population – prophylactic treatment
Lee 2014[29]	Inappropriate comparison – shunting techniques
Lesniak 2002[30]	Inappropriate study design – non comparative
Lewis 2016[31]	Inappropriate outcome – vasospasm at baseline
Lin 1999[32]	Inappropriate study design – predictive factors of poor outcome
Little 2008[33]	Inappropriate comparison – wall thickness
Lu 2012[34]	Inappropriate study design – non comparative
Maeda 2013[35]	Inappropriate population – majority non hydrocephalus
Manet 2016[37]	Inappropriate study design – non comparative
Manet 2017[36]	Inappropriate population – majority traumatic brain injury
Mori 2001[38]	Inappropriate population – SAH excluded
Moriyama 1995[39]	Inappropriate population – hydrocephalus prophylaxis
Murakami 2007[40]	Inappropriate study design - response to shunting
Nee 2017[42]	Inappropriate population – majority non hydrocephalus
Ormond 2013[44]	Inappropriate study design – non comparative

Reference	Reason for exclusion
Otawara 2007[45]	Inappropriate population – prophylactic treatment
Park 2015[46]	Inappropriate population – prophylactic treatment
Peng 2016[47]	Inappropriate population – chronic subdural haematoma
Phillips 2014[48]	Inappropriate study design – non comparative
Poon 2008[49]	Inappropriate study design – non comparative (no adjustment)
Qian 2016[50]	Systematic review: references screened
Reddy 2011[52]	Inappropriate study design – non comparative
Reddy 2012[51]	Inappropriate study design – non comparative
Roitberg 2001[53]	Inappropriate comparison – prophylactic treatment
Sasaki 2004[54]	Inappropriate population – non hydrocephalus
Speck 2011[55]	Inappropriate outcome – diagnostic accuracy
Steinke 1987[56]	Inappropriate study design – non comparative (no adjustment)
Sun 2014[57]	Inappropriate population – prophylactic treatment
Takeuchi 2015[58]	Inappropriate population – majority non hydrocephalus
Thenier-Villa 2020[59]	Inappropriate comparison – rebleeding compared to no bleeding (all with EVD)
Wen 2015[60]	Inappropriate population – traumatic brain injury
Woernle 2013[61]	Inappropriate outcome – predictive factors for shunt treatment
Yilmazlar 2005[62]	Inappropriate comparison – single vs multiple EVD
Yoshimoto 1998[63]	Inappropriate comparison – SAH compared to non SAH
Zhao 2015[65]	Inappropriate study design – non comparative (no adjustment)

J.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 13: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	