National Institute for Health and Care Excellence

Draft

Head injury: assessment and early management (update)

[J] Evidence review for admission and observation of people with concussion symptoms

NICE guideline < number>

Evidence reviews underpinning recommendations x to y and research recommendations in the NICE guideline

September 2022

Draft for Consultation

These evidence reviews were developed by the Guideline Development Team NGC



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1 Admission and observation of people

with concussion symptoms after normal

- brain imaging or no indication for early
- 4 imaging

5 1.1 Review question

- 6 Should people with concussion symptoms be admitted or discharged from hospital after
- 7 normal brain imaging or no indication for early imaging?

1.1.1 Introduction

8

- 9 It is estimated there are approximately 1.4 million attendances to Emergency Departments in
- 10 England and Wales each year from individuals who have suffered a recent head injury.
- Around 95% of those presenting will have a GCS of 13/15, or higher, and either do not
- 12 require neuroimaging or undergo neuroimaging which does not reveal any evidence of a
- recent significant structural brain injury. Despite this, many of these people will report
- 14 symptoms of concussion. At present the observation and admission of these individuals is
- 15 based on clinical judgement. This guideline has reviewed the evidence for the admission and
- observation of people with concussion.

17 **1.1.2 Summary of the protocol**

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

19 Table 1: PICO characteristics of review question

Population	Admission and observation of people with concussion symptoms Inclusion: -Infants, children and adult with people with concussion symptoms after normal
	brain imaging or no indication for early imaging -People who are GCS 15
	Strata: • Adults (aged ≥16 years) • Children (aged ≥1 to <16 years) • Infants (aged <1 year)
	Exclusion: Adults and children (including infants under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury. Those with GCS <15, even if baseline GCS is already <15
Intervention	Admission
	Where only indication for admission is that they have symptoms of concussion either with normal imaging (CT/MR imaging) or no indications for imaging.

Comparison	Discharge
	After normal imaging (CT/MR imaging) or no indications for imaging.
Outcomes	 Time to diagnosis of intracranial injury on CT/MRI/clinical follow-up or autopsy Quality of life (at least 3 months) Re-admission as a result of delayed diagnosis of intracranial injury within 4 weeks Traumatic brain injury (TBI) related mortality Objectively applied score of disability e.g., Glasgow Outcome Score (GOS) or extended GOS - at 3 months or more Return to work/study/usual activities Post-concussion outcomes: ongoing cognitive difficulties, RPQ measure of post-concussion symptoms Mental health measures e.g. SDQ, Birrleson Depression and Anxiety
	scales, PHQ, GAD
Study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders, starting with prospective cohort studies. Key confounders: No key confounders were identified as the population was considered to be very specific as people should not have any other indications for admission

1

2

1.1.3 Methods and process

- This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.
- 5 Declarations of interest were recorded according to <u>NICE's conflicts of interest policy</u>.

1 1.1.4 Effectiveness evidence

2 1.1.4.1 Included studies

- 3 No relevant clinical studies comparing admission to discharge after normal imaging (CT/MR
- 4 imaging) or no indications for imaging were identified.
- 5 See also the study selection flow chart in Appendix C, study evidence tables in Appendix D,
- 6 forest plots in Appendix E and GRADE tables in Appendix F.

7 1.1.4.2 Excluded studies

- 8 See the excluded studies list in Appendix J.
- 9 1.1.5 Summary of studies included in the effectiveness evidence
- 10 No evidence was identified.
- 1.1.6 Summary of the effectiveness evidence
- 12 No evidence was identified.
- 13 **1.1.7 Economic evidence**
- 14 1.1.7.1 Included studies
- No health economic studies were included.
- 16 **1.1.7.2 Excluded studies**
- 17 No relevant health economic studies were excluded due to assessment of limited
- 18 applicability or methodological limitations.
- 19 See also the health economic study selection flow chart in Appendix G.

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- 1 1.1.8 Summary of included economic evidence
- 2 None
- 3 1.1.9 Economic model
- 4 Modelling was not conducted for this review.

1 **1.1.10 Unit costs**

National Schedule of NHS Costs - Year 2019-20 version 2 - NHS trusts and NHS foundation trusts NON ELECTIVE SHORT STAY				
Code	Description	Number of Finished consultant episodes	National Average Unit Cost	
AA26C	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 15+	5,469	£1,256	
AA26D	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 12-14	8,639	£654	
AA26E	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 9-11	14,996	£580	
AA26F	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 6-8	23,237	£520	
AA26G	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 3-5	33,460	£465	
AA26H	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 0-2	31,230	£386	
AA26	Weighted average	117,031	£521	

2 1.1.11 Evidence statements

3 **Economic**

• No relevant economic evaluations were identified.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

- 3 The committee considered all outcomes as equally important for decision making and
- 4 therefore have all been rated as critical: time to diagnosis of intracranial injury on
- 5 CT/MRI/clinical follow-up or autopsy; quality of life; re-admission as a result of delayed
- 6 diagnosis of intracranial injury within 4 weeks; traumatic brain injury (TBI) related mortality;
- 7 objectively applied score of disability e.g. Glasgow Outcome Score (GOS) or extended GOS
- 8 (GOS-E) at 3 months or more; return to work/study/usual activities; post-concussion
- 9 outcomes: ongoing cognitive difficulties, The Rivermead Post-Concussion Symptoms
- 10 Questionnaire (RPQ) measure of post-concussion symptoms; and mental health measures
- 11 (e.g. The strengths and difficulties questionnaire (SDQ), Birrleson Depression and Anxiety
- scales, Patient Health Questionnaire (PHQ), Generalised Anxiety Disorder Assessment
- 13 (GAD).

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14 No evidence was identified for any of the outcomes.

15 **1.1.12.2 The quality of the evidence**

No evidence was identified in adults, infants and children.

1.1.12.3 Benefits and harms

- 18 The committee discussed that currently, there is uncertainty whether those presenting with
- 19 concussion symptoms should be admitted or discharged after normal brain imaging or no
- 20 indication for early imaging. The committee agreed to focus this review on concussion
- 21 symptoms in people presenting early in the pathway as post-concussion syndrome can only
- 22 be identified at least weeks after injury.
- 23 Concussion symptoms in adults and children include: headache, dizziness, nausea,
- amnesia, clumsiness or trouble with balance, altered cognition, feeling stunned, dazed or
- confused, changes in vision –such as blurred vision, double vision or "seeing stars", "being
- 26 knocked out" or struggling to stay awake. Some additional symptoms may present in
- 27 children: changes in their normal behaviour after a head injury, such as crying a lot or
- 28 irritability, differences in their feeding or sleeping habits or a loss of interest in people or
- 29 objects. This population will have GCS 15.

30 Adults, children and infants:

- 31 There was no evidence for admission or discharge of people with concussion symptoms after
- 32 normal imaging or no indication for imaging. The committee discussed that the main
- 33 objective of admission of people with concussion symptoms with normal imaging or no
- indication for imaging is to observe if they develop any complications.
- 35 The committee discussed that in current practice discharge of adults, children and infants
- with concussion symptoms after normal imaging or no indication for imaging is based on
- 37 clinical discretion. Admission is considered if non-accidental injury is suspected. Current
- practice is variable. Some people are admitted to hospital overnight for observation only (no
- 39 active treatment is offered during the hyperacute phase) while most people with concussion
- 40 symptoms are discharged for home observation after initial observation in the hospital if they
- 41 have normal CT, have no neurological signs, cleared post-traumatic amnesia (PTA), and
- have someone to look after them at home and check on them for at least 24 hours to ensure
- 43 that their symptoms are not worsening. They are advised to rest in a quiet environment along
- with a follow-up appointment with the neuro trauma unit/GP within 2 weeks to monitor the
- symptoms. When people with concussion symptoms are discharged, information is provided
- on when to return to hospital to seek further immediate care and ongoing support for
- 47 persistent symptoms (see recommendations on discharge advice 1.9.8 and 1.9.13). From

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Admission and observation of people with concussion

- 1 their experience the committee stated that majority of people with concussion symptoms and
- 2 normal imaging do not need further intervention and are safe to be discharged from the
- 3 emergency department (ED).
- 4 The committee however did not consider it appropriate to make consensus
- 5 recommendations in the context of lack of evidence specifically for people with concussion
- 6 symptoms.
- 7 The committee highlighted that current practice is to not admit people with concussion
- 8 symptoms unless they have any of the indications in recommendations 1.8.1. The
- 9 committee were unaware of any evidence indicating that current practice was causing harm
- 10 (coroners reports, safety reports, patient group feedback). They noted that admission has the
- potential to make people worse for example being in a noisy and unfamiliar ward
- 12 environment and could increase the risk of nosocomial infections. The committee did not
- 13 consider it appropriate to make consensus recommendations specifically for people with
- 14 concussion symptoms but added a cross reference to the recommendations on the criteria
- 15 for performing a head CT.
- 16 The committee did not want to make any research recommendation on this topic as in
- 17 current practice these people are not admitted. There is no evidence (e.g. from coroners
- reports, safety reports, patient groups) to suggest that this current policy is causing any harm
- 19 to this group.

1.1.12.4 Cost effectiveness and resource use

- 21 Concussion and post-concussion syndrome represent a substantial burden on patients and
- the NHS. However, admitting and observing people with concussion straight after the injury
- is not common practice unless there are other indfications for admission. Routine admission
- 24 would use up valuable beds and staff time that might be more usefully spent on other
- 25 patients.

20

- No economic evaluations were identified for this review, therefore the unit costs of a short
- admision was presented to aid committee consideration of cost effectiveness.
- 28 In the absence of clinical effectiveness evidence, it's uncertain whether patient outcomes
- 29 would be improved by admission and observation. Therefore cost effectiveness is also
- 30 uncertain. However, the committee decided that research funding would be better spent on
- 31 other questions.

32 1.1.12.5 Other factors the committee took into account

33 None.

34

References

- 2 National Institute for Health and Care Excellence. Developing NICE guidelines: the manual [updated January 2022]. London; 2014. Available from:
- 3 https://www.nice.org.uk/process/pmg20/chapter/introduction 4

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Appendices

2 Appendix A – Review protocols

3 Review protocol for admission and observation of people with concussion

ID	Field	Content	
0.	PROSPERO registration number	CRD42021282627	
1.	Review title	Admission and observation of people with concussion symptoms after normal brain imaging or no indication for early imaging	
		Concussion symptoms include:	
		Symptoms in adults	
		headache	
		• dizziness	
		• nausea	
		amnesia	
		clumsiness or trouble with balance	
		Altered cognition, feeling stunned, dazed or confused (as long as GCS is 15)	
		changes in your vision – such as blurred vision, double vision or "seeing stars"	
		being knocked out or struggling to stay awake	
		Additional symptoms that may present in children	
		changes in their normal behaviour after a head injury, such as:	
		crying a lot or irritability	

		differences in their feeding or sleeping habits
		a loss of interest in people or objects
2.	Review question	3.2) Should people with concussion symptoms be admitted or discharged from hospital after normal brain imaging or no indication for early imaging?
3.	Objective	To determine if people with concussion symptoms be admitted or discharged from hospital after normal brain imaging or no indication for early imaging.
4.	Searches	The following databases (from inception) will be searched:
		Cochrane Central Register of Controlled Trials (CENTRAL)
		Cochrane Database of Systematic Reviews (CDSR)
		• Embase
		MEDLINE
		Epistemonikos
		Searches will be restricted by:
		English language studies
		Human studies
		Other searches:
		Inclusion lists of systematic reviews
		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. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5. Condition or domain being studied	Admission and observation of people with concussion symptoms
6. Population	 i) Inclusion: Infants, children and adult with concussion symptoms after normal brain imaging or no indication for early imaging ii) People who are GCS 15 Strata (i): Adults (aged ≥16 years) Children (aged ≥1 to <16 years) and infants(aged <1 year) Mixed population studies will be included but downgraded for indirectness. Cut-off of 60% will be used for all age groups Exclusion: Adults, and children (including infants under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury. Those with Glasgow Coma Scale (GCS) score <15, even if baseline GCS is already <15

7.	Intervention	Admission
		Where only indication for admission is that they have symptoms of concussion either with normal imaging (CT/MR imaging) or no indications for imaging.
		Definition of admission could vary (would be an admission to hospital, but may not always be to a ward) – report definition used in each study.
		Report what happened in each study when they were admitted (e.g. observation/assessment) and the duration of the admission in each study
8.	Comparator	Discharge
		After normal imaging (CT/MR imaging) or no indications for imaging.
9.	Types of study to be included	Randomised controlled trials (RCTs), systematic reviews of RCTs.
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	If no RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders, starting with prospective cohort studies.
		Key confounders: No key confounders were identified as the population was considered to be very specific as people should not have any other indications for admission
10.	Other exclusion criteria	Non-English language studies.
		Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.

		Non-comparative studies.
11.	Context	There is uncertainty about whether those presenting with concussion symptoms should be admitted or discharged. Although the draft scope question was specifically in those with post-concussion syndrome, the committee agreed that this area would be sufficiently covered by prognostic reviews on the guideline and agreed to focus this intervention review on concussion symptoms in people presenting early in the pathway.
12.	Primary outcomes (critical outcomes)	Time to diagnosis of intracranial injury on CT/MRI/clinical follow-up or autopsy
		Quality of life (at least 3 months)
		Re-admission as a result of delayed diagnosis of intracranial injury within 4 weeks
		TBI related mortality
		 Objectively applied score of disability e.g. Glasgow Outcome Score (GOS) or extended GOS - at 3 months or more
		Return to work/study/usual activities
		 Post-concussion outcomes: ongoing cognitive difficulties, RPQ measure of post- concussion symptoms
		 Mental health measures e.g. SDQ, Birrleson Depression and Anxiety scales, patient health questionnaire (PHQ), generalised anxiety disorder (GAD)
		TBI mortality no time limit, report as per papers Return to work or study any time period up to one year (admission may both delay return to work bec pt in hospital, but also hasten return if an intracranial injury is detected), report as per papers
		Post-concussion symptoms -time course does not matter because it's unlikely that admission (i.e. the intervention) is going to prevent post-concussion symptoms. Report as per papers.
		Outcomes will be grouped:< 6 months and ≥ 6 months

13.	Data extraction (selection and coding)	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.
		A standardised form will be used to extract data from studies (see <u>Developing NICE guidelines: the manual</u> section 6.4).
		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.
14.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.
		For Intervention reviews
		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

15.	Strategy for data synthesis	 Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. Heterogeneity between the studies in effect measures will be assessed using the I² statistic and visually inspected. An I² value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. 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. The risk of bias across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.
16.	Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: • Imaging performed before admission/discharge: • Normal imaging • No indication for early imaging

		For children stratum	
			o Preschool age (≤5 years)
			o >5 years
17.	Type and method of review	\boxtimes	Intervention
			Diagnostic
			Prognostic
			Qualitative
			Epidemiologic
			Service Delivery
			Other (please specify)
18.	Language	English	
19.	Country	England	
20.	Anticipated or actual start date	[For the purposes of PROSPERO, the date of commencement for the systematic review can be defined as any point after completion of a protocol but before formal screening of the identified studies against the eligibility criteria begins.	
		A protocol cassurance.]	an be deemed complete after sign-off by the NICE team with responsibility for quality
21.	Anticipated completion date	[Give the date by which the guideline is expected to be published. This field may be edited at any time. All edits will appear in the record audit trail. A brief explanation of the reason for changes should be given in the Revision Notes facility.]	

22.	Stage of review at time of this	Review stage	Started	Completed
	submission	Preliminary searches	V	
		Piloting of the study selection process		
		Formal screening of search results against eligibility criteria		
		Data extraction		
		Risk of bias (quality) assessment		
		Data analysis		
23.	Named contact	5a. Named contact		
		National Guideline C	entre	
		5e Organisational aff	ce.org.uk with Guidelii iliation of the	ne Coordinator for email address] e review Care Excellence (NICE) and [National Guideline Alliance /
				E Guideline Updates Team / NICE Public Health Guideline

		Development Team] [Note it is essential to use the template text here and one of the centre options to enable PROSPERO to recognise this as a NICE protocol]	
24.	Review team members	[Give the title, first name, last name and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.]	
		From the National Guideline Centre:	
		[Guideline lead]	
		[Senior systematic reviewer]	
		Systematic reviewer	
		[Health economist]	
		[Information specialist]	
		[Others]	
25.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.	
26.	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.	
27.	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: [NICE guideline webpage].	

	1		
28.	Other registration details	[Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.]	
29.	Reference/URL for published protocol	[Give the citation and link for the published protocol, if there is one.]	
30.	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.	
		[Add in any additional agree dissemination plans.]	
31.	Keywords	Post-concussion syndrome, follow-up, discharge	
32.	Details of existing review of same topic by same authors	NA	
33.	Current review status	□ Ongoing	
İ		□ Completed but not published	
		□ Completed and published	
		□ Completed, published and being updated	
		□ Discontinued	
34.	Additional information	[Provide any other information the review team feel is relevant to the registration of the review.]	
35.	Details of final publication	www.nice.org.uk	

1

2 Table 2: Health economic review protocol

Review question	All questions – health economic evidence
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 – see appendix B below. The search covered all years
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2006, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2006 or later that were included in the previous guidelines will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. 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 (2014).(1) 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 make a decision 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 on the basis of 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 2006 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2006 will be rated as 'Not applicable'.

• Studies published before 2006 (including any such studies included in the previous guidelines) 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

1 Appendix B – Literature search strategies

- 2 The literature searches for this review are detailed below and complied with the methodology
- 3 outlined in Developing NICE guidelines: the manual.(1)
- 4 For more information, please see the Methodology review published as part of the
- 5 accompanying documents for this guideline.

B.4 Clinical search literature search strategy

- 7 Searches were constructed using a PICO framework where population (P) terms were
- 8 combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are
- 9 rarely used in search strategies as these concepts may not be indexed or described in the
- 10 title or abstract and are therefore difficult to retrieve.

11 Table 3: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Randomised controlled trials Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	Randomised controlled trials Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
The Cochrane Library (Wiley)	Cochrane Reviews to 2022 Issue 6 of 12 CENTRAL to 2022 Issue 6 of 12	
Epistemonikos (The Epistemonikos Foundation)	Inception to 22 June 2022	Exclusions (Cochrane reviews)

12 Medline (Ovid) search terms

1.	exp Brain Concussion/
2.	(concuss* or postconcuss* or PCSS).ti,ab.
3.	((mild or minor) adj2 (head or brain) adj2 (injur* or trauma*)).ti,ab.
4.	(mild TBI or mTBI).ti,ab.
5.	or/1-4
6.	letter/
7.	editorial/

8.	news/
9.	exp historical article/
10.	Anecdotes as Topic/
11.	comment/
12.	case report/
13.	(letter or comment*).ti.
14.	or/6-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animals/ not humans/
18.	exp Animals, Laboratory/
19.	exp Animal Experimentation/
20.	exp Models, Animal/
21.	exp Rodentia/
22.	(rat or rats or mouse or mice or rodent*).ti.
23.	or/16-22
24.	5 not 23
25.	limit 24 to English language
26.	(admit* or admission* or observation* or hospitali#ation).ti,ab.
27.	hospitalization/ or patient admission/
28.	discharg*.ti,ab.
29.	(follow-up* or followup* or monitor*).ti,ab.
30.	patient discharge/ or patient handoff/
31.	patient care/ or ambulatory care/ or "continuity of patient care"/ or patient transfer/ or retention in care/
32.	(ED or ER or "accident and emergency" or "A&E" or MTC).ti,ab.
33.	(trauma adj2 (centre* or center* or unit* or department* or dept*)).ti,ab.
34.	(emergency adj2 (department* or dept* or unit* or room* or hospital* or ward* or centre* or center*)).ti,ab.
35.	exp Emergency Service, Hospital/
36.	or/26-35
37.	25 and 36
38.	randomized controlled trial.pt.
39.	controlled clinical trial.pt.
40.	randomi#ed.ti,ab.
41.	placebo.ab.
42.	randomly.ti,ab.
43.	Clinical Trials as topic.sh.
44.	trial.ti.
45.	or/38-44
46.	Meta-Analysis/
47.	exp Meta-Analysis as Topic/
48.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
49.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
50.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.

	1
51.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
52.	(search* adj4 literature).ab.
53.	(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.
54.	cochrane.jw.
55.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
56.	or/46-55
57.	Epidemiologic studies/
58.	Observational study/
59.	exp Cohort studies/
60.	(cohort adj (study or studies or analys* or data)).ti,ab.
61.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
62.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
63.	Controlled Before-After Studies/
64.	Historically Controlled Study/
65.	Interrupted Time Series Analysis/
66.	(before adj2 after adj2 (study or studies or data)).ti,ab.
67.	exp case control study/
68.	case control*.ti,ab.
69.	Cross-sectional studies/
70.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
71.	or/57-70
72.	37 and (45 or 56 or 71)

13 Embase (Ovid) search terms

exp brain concussion/ concuss* or postconcuss* or PCSS).ti,ab.
concluse* or postconcluse* or PCSS) tilah
concuss of postconcuss of rossy.ti,ab.
(mild or minor) adj2 (head or brain) adj2 (injur* or trauma*)).ti,ab.
mild TBI or mTBI).ti,ab.
or/1-4
etter.pt. or letter/
note.pt.
editorial.pt.
conference abstract or conference paper).pt.
case report/ or case study/
letter or comment*).ti.
or/6-11
andomized controlled trial/ or random*.ti,ab.
12 not 13
animal/ not human/
nonhuman/
exp Animal Experiment/
exp Experimental Animal/
animal model/

20.	exp Rodent/
21.	(rat or rats or mouse or mice or rodent*).ti.
22.	or/14-21
23.	5 not 22
24.	limit 23 to English language
25.	(admit* or admission* or observation* or hospitali#ation).ti,ab.
26.	*hospitalization/
27.	discharg*.ti,ab.
28.	(follow-up* or followup* or monitor*).ti,ab.
29.	*hospital discharge/
30.	*clinical handover/
31.	*patient care/
32.	*ambulatory care/
33.	*retention in care/
34.	*patient transport/
35.	(ED or ER or "accident and emergency" or "A&E" or MTC).ti,ab.
36.	*hospital emergency service/
37.	*emergency health service/
38.	(trauma adj2 (centre* or center* or unit* or department* or dept*)).ti,ab.
39.	(emergency adj2 (department* or dept* or unit* or room* or hospital* or ward* or centre* or center*)).ti,ab.
40.	or/25-39
41.	24 and 40
42.	random*.ti,ab.
43.	factorial*.ti,ab.
44.	(crossover* or cross over*).ti,ab.
45.	((doubl* or singl*) adj blind*).ti,ab.
46.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
47.	crossover procedure/
48.	single blind procedure/
49.	randomized controlled trial/
50.	double blind procedure/
51.	or/42-50
52.	systematic review/
53.	Meta-Analysis/
54.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
55.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
56.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
57.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
58.	(search* adj4 literature).ab.
59.	(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.
60.	cochrane.jw.
61.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

62.	or/52-61
63.	Clinical study/
64.	Observational study/
65.	Family study/
66.	Longitudinal study/
67.	Retrospective study/
68.	Prospective study/
69.	Cohort analysis/
70.	Follow-up/
71.	cohort*.ti,ab.
72.	70 and 71
73.	(cohort adj (study or studies or analys* or data)).ti,ab.
74.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
75.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
76.	(before adj2 after adj2 (study or studies or data)).ti,ab.
77.	exp case control study/
78.	case control*.ti,ab.
79.	cross-sectional study/
80.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
81.	or/63-69,72-80
82.	41 and (51 or 62 or 81)

14 Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Brain Concussion] explode all trees
#2.	(concuss* or postconcuss* or PCSS):ti,ab
#3.	((mild or minor) NEAR/2 (head or brain) NEAR/2 (injur* or trauma*)):ti,ab
#4.	(mild TBI or mTBI):ti,ab
#5.	#1 or #2 or #3 or #4
#6.	(admit* or admission* or observation* or hospitali?ation):ti,ab
#7.	MeSH descriptor: [Hospitalization] this term only
#8.	MeSH descriptor: [Patient Admission] this term only
#9.	discharg*:ti,ab
#10.	(follow-up* or followup* or monitor*):ti,ab
#11.	MeSH descriptor: [Patient Discharge] this term only
#12.	MeSH descriptor: [Patient Handoff] this term only
#13.	MeSH descriptor: [Patient Care] this term only
#14.	MeSH descriptor: [Ambulatory Care] this term only
#15.	MeSH descriptor: [Continuity of Patient Care] this term only
#16.	MeSH descriptor: [Patient Transfer] this term only
#17.	MeSH descriptor: [Retention in Care] this term only
#18.	(ED or ER or "accident and emergency" or "A&E" or MTC):ti,ab
#19.	MeSH descriptor: [Emergency Service, Hospital] explode all trees
#20.	(trauma NEAR/2 (centre* or center* or unit* or department* or dept*)):ti,ab

#21.	(emergency NEAR/2 (department* or dept* or unit* or room* or hospital* or ward* or centre* or center*)):ti,ab
#22.	#6 or #7 or #8 or #9 or #10 or #11 OR #12 OR #13 or #14 or #15 or #16 or #17 or #18 OR #19 OR #20 OR #21
#23.	#5 AND #22

15 Epistemonikos search terms

1.	(advanced_title_en:((concuss* OR postconcuss* OR PCSS)) OR
	advanced_abstract_en:((concuss* OR postconcuss* OR PCSS))) OR
	(advanced_title_en:(((mild OR minor) AND (head OR brain) AND (injur* OR trauma*)))
	OR advanced abstract en:(((mild OR minor) AND (head OR brain) AND (injur* OR
	trauma*)))) AND (advanced_title_en:((admit* OR admission* OR observation* OR
	monitor* OR hospitalization OR hospitalisation OR discharg* OR followup* OR follow-
	up* OR emergency OR trauma)) OR advanced abstract en:((admit* OR admission*
	OR observation* OR monitor* OR hospitalization OR hospitalisation OR discharg* OR
	followup* OR follow-up* OR emergency OR trauma)))

Bi ≥ Health Economics literature search strategy

- 17 Health economic evidence was identified by conducting searches using terms for a broad
- Head Injury population. The following databases were searched: NHS Economic Evaluation
- 19 Database (NHS EED this ceased to be updated after 31st March 2015), Health Technology
- 20 Assessment database (HTA this ceased to be updated from 31st March 2018) and The
- 21 International Network of Agencies for Health Technology Assessment (INAHTA). Searches
- 22 for recent evidence were run on Medline and Embase from 2014 onwards for health
- 23 economics, and all years for quality-of-life studies.

24 Table 4: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022 Quality of Life 1946 – 22 June 2022	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies Exclusions (animal studies,
	Quality of Life 1974 – 22 June 2022	letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31st March 2015	
Health Technology Assessment Database (HTA)	Inception – 31st March 2018	

Database	Dates searched	Search filters and limits applied
(Centre for Research and Dissemination – CRD)		
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

25 Medline (Ovid) search terms

1.	craniocerebral trauma/ or exp brain injuries/ or coma, post-head injury/ or exp head injuries, closed/ or head injuries, penetrating/ or exp intracranial hemorrhage, traumatic/ or exp skull fractures/
2.	((skull or cranial) adj3 fracture*).ti,ab.
3.	((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.
5.	or/1-4
6.	letter/
7.	editorial/
8.	news/
9.	exp historical article/
10.	Anecdotes as Topic/
11.	comment/
12.	case report/
13.	(letter or comment*).ti.
14.	or/6-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animals/ not humans/
18.	exp Animals, Laboratory/
19.	exp Animal Experimentation/
20.	exp Models, Animal/
21.	exp Rodentia/
22.	(rat or rats or mouse or mice or rodent*).ti.
23.	or/16-22
24.	5 not 23
25.	limit 24 to English language
26.	economics/
27.	value of life/
28.	exp "costs and cost analysis"/
29.	exp Economics, Hospital/
30.	exp Economics, medical/
31.	Economics, nursing/

32.	economics, pharmaceutical/
33.	exp "Fees and Charges"/
34.	exp budgets/
35.	budget*.ti,ab.
36.	cost*.ti.
37.	(economic* or pharmaco?economic*).ti.
38.	(price* or pricing*).ti,ab.
39.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
40.	(financ* or fee or fees).ti,ab.
41.	(value adj2 (money or monetary)).ti,ab.
42.	or/26-41
43.	quality-adjusted life years/
44.	sickness impact profile/
45.	(quality adj2 (wellbeing or well being)).ti,ab.
46.	sickness impact profile.ti,ab.
47.	disability adjusted life.ti,ab.
48.	(qal* or qtime* or qwb* or daly*).ti,ab.
49.	(euroqol* or eq5d* or eq 5*).ti,ab.
50.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/43-61
63.	25 and (42 or 62)

26 Embase (Ovid) search terms

1.	head injury/
2.	exp brain injury/
3.	skull injury/ or exp skull fracture/
4.	((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.

7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	(conference abstract or conference paper).pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/8-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	
24.	(rat or rats or mouse or mice or rodent*).ti.
25.	7 not 24
26.	
27.	limit 25 to English language health economics/
28.	
29.	exp economic evaluation/
30.	exp health care cost/
31.	exp fee/
32.	budget/
	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37. 38.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/27-39
41.	quality-adjusted life years/
42.	"quality of life index"/
43.	short form 12/ or short form 20/ or short form 36/ or short form 8/
44.	sickness impact profile/
45.	(quality adj2 (wellbeing or well being)).ti,ab.
46.	sickness impact profile.ti,ab.
47.	disability adjusted life.ti,ab.
48.	(qal* or qtime* or qwb* or daly*).ti,ab.

49.	(euroqol* or eq5d* or eq 5*).ti,ab.
50.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/41-61
63.	26 and (40 or 62)

27 NHS EED and HTA (CRD) search terms

MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
MeSH DESCRIPTOR Craniocerebral Trauma
MeSH DESCRIPTOR Coma, Post-Head Injury
MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
MeSH DESCRIPTOR Head Injuries, Penetrating
MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
(((skull or cranial) adj3 fracture*))
(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

28 INAHTA search terms

1.	((((trauma* and ((subdural or intracranial or brain) and (haematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title]) AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title])) OR ((((skull or cranial) and fracture*))[Title] OR (((skull or cranial) and fracture*))[abs]) OR ((((head or brain or craniocerebral or intracranial or cranial or skull) and (injur* or trauma*)))[Title] OR (((head or brain or craniocerebral or intracranial or cranial or skull) and (injur* or trauma*)))[abs]) OR ("Skull Fractures"[mhe]) OR ("Intracranial Hemorrhage, Traumatic"[mhe]) OR ("Head Injuries, Penetrating"[mh]) OR ("Head Injuries, Closed"[mhe]) OR ("Coma, Post-Head Injury"[mh]) OR ("Brain Injuries"[mhe]) OR ("Craniocerebral Trauma"[mh])
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30

31

32

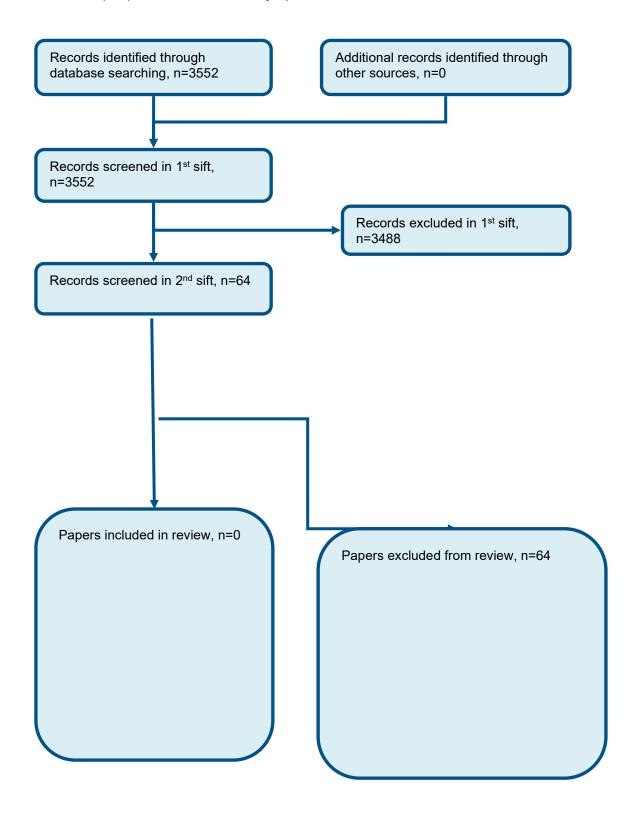
33 34

35 36

37

Appendix C – Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of admission and observation of people with concussion symptoms



- Appendix D Effectiveness evidence
- 2 No evidence was identified.

- 3 Forest plots
- 4 No evidence was identified

Appendix E – Economic evidence study selection

2 Records identified through database Additional records identified through other sources: searching (after de-duplication), CG176, n=3 n=1658 Clinical review, n=4 Records screened in 1st sift, n=1665 Records excluded* in 1st sift, n=1620 Full-text papers assessed for eligibility in 2nd sift, n=45 Papers excluded* in 2nd sift, n=29 Full-text papers assessed for applicability and quality of methodology, n=16 Papers selectively excluded, Papers included, n=9 Papers excluded, n=3 (6 studies) • 1.1 Tranexamic: n=0 • 1.1 Tranexamic: n=3 (2 • 1.1 Tranexamic: n=0 studies) • 1.2 Bypass: n=1 • 1.2 Bypass: n=0 • 1.2 Bypass: n=1 • 1.3 Direct imaging: n=0 • 1.3 Direct imaging: n=0 • 1.3 Direct imaging: n=0 • 2.1a Prediction rules: n=4 • 2.1a Prediction rules: • 2.1a Head CT rules: n=4 • 2.1b Head CT rules in (2 studies) • 2.1b Head CT rules in subgroups: n=0 • 2.1b Head CT rules in subgroups: n=0 • 2.2 MRI & biomarkers for subgroups: n=1 PCS=0 • 2.2 MRI & biomarkers for • 2.2 MRI & biomarkers for PCS=0 • 2.3 Biomarkers for PCS=0 · 2.3 Biomarkers for complications n=0 • 2.3 Biomarkers for complications n=1 • 2.4 C-spine: n=0 complications n=0 • 2.4 C-spine: n=0 • 3.1-3.3 Admission n=0 • 2.4 C-spine: n=0 • 3.1-3.3 Admission n=0 • 3.4-3.5 hypopituitarism=0 • 3.1-3.3 Admission n=0 • 3.4-3.5 hypopituitarism=0 3.6 Isolated skull • 3.4-3.5 hypopituitarism=0 fracture=0 • 3.6 Isolated skull • 3.6 Isolated skull fracture=0 fracture=0

1

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

1 Appendix F – Economic evidence tables

3 None.

2

1 Appendix G – Excluded studies

2 Clinical studies

3 Table 4: Studies excluded from the clinical review

Study	Code [Reason]
Adams, J., Frumiento, C., Shatney-Leach, L. et al. (2001) Mandatory admission after isolated mild closed head injury in children: is it necessary?. Journal of Pediatric Surgery 36(1): 119-21	- No comparison group
af Geijerstam, J. L. and Britton, M. (2005) Mild head injury: reliability of early computed tomographic findings in triage for admission. Emergency Medicine Journal 22(2): 103-7	Review article but not a systematic reviewConference abstract
Af Geijerstam, J. L.; Britton, M.; Marke, L. A. (2004) Mild head injury: observation or computed tomography? Economic aspects by literature review and decision analysis. Emergency Medicine Journal 21(1): 54-8	- HE paper
af Geijerstam, J. L., Oredsson, S., Britton, M. et al. (2006) Medical outcome after immediate computed tomography or admission for observation in patients with mild head injury: randomised controlled trial. BMJ 333(7566): 465	- Study does not contain an intervention relevant to this review protocol Study compared CT vs observation strategy
af Geijerstam, J.; Oredsson, S.; Britton, M. (2005) OCTOPUS observation or computed tomography of mild head injury in Sweden: a randomised clinical trial concerning effects and costs. Critical care (london, england) 9(suppl1)	- Conference abstract
af Geijerstam, J.; Oredsson, S.; Britton, M. (2005) Mild Head Injury - Computed Tomography or Inhospital Observation? A Randomized Controlled Trial Concerning Effects and Costs. Annals of emergency medicine 46(suppl3): 109-110	- Study does not contain an intervention relevant to this review protocol Study compared CT vs in-hospital observation
Anderson, V., Rausa, V. C., Anderson, N. et al. (2021) Protocol for a randomised clinical trial of multimodal postconcussion symptom treatment and recovery: the Concussion Essentials study. BMJ Open 11(2): e041458	- Protocol Protocol for a RCT for treatment of post- concussion symptoms in children
Andreassen, J., Bach-Nielsen, P., Heckscher, H. et al. (1957) Reassurance and short period of	- Article

Study	Code [Reason]
bed rest in the treatment of concussion; follow- up and comparison with results in other series treated by prolonged bed rest. Acta Medica Scandinavica 158(34): 239-48	
Anonymous (2013) Study: observation is a good strategy when caring for children who present with minor blunt head trauma. ED Management 25(11): 129-31	- Study does not contain an intervention relevant to this review protocol Study aims to determine if children who present to the ED with minor blunt head trauma benefit from a period of observation before physicians decide whether to order computed tomography (CT) scan.
Arienta, C.; Caroli, M.; Balbi, S. (1997) Management of head-injured patients in the emergency department: a practical protocol. Surgical Neurology 48(3): 213-9	- Study does not contain an intervention relevant to this review protocol Practical protocol for management of head inured patients in ED.
Baglaj, M.; Czernik, J.; Ladogorska, J. (2005) Minor head injuries in children - Are radiological examinations and hospitalization necessary in every case?. [Polish, English]. Polski Przeglad Chirurgiczny 77(7): 672-689	- Study does not contain an intervention relevant to this review protocol Study aims to retrospectively analyse diagnostic and clinical management with minor head injuries. No comparison group.
Bazarian, J.; Hartman, M.; Delahunta, E. (2000) Minor head injury: Predicting follow-up after discharge from the emergency department. Brain Injury 14(3): 285-294	- Study does not contain an intervention relevant to this review protocol Study aims to identify factors predicting follow-up after ED discharge.
Brooks, T. M., Smith, M. M., Silvis, R. M. et al. (2017) Symptom-Guided Emergency Department Discharge Instructions for Children With Concussion. Pediatric Emergency Care 33(8): 553-563	- Study does not contain an intervention relevant to this review protocol study evaluates the use and utility of a novel set of ED discharge instructions.
Brown, S. R., Raine, C., Robertson, C. E. et al. (1994) Management of minor head injuries in the accident and emergency department: the effect of an observation ward. Journal of Accident & Emergency Medicine 11(3): 144-8	- Inappropriate intervention and comparator Study compared the management of patients presenting with minor head injury to the A&E departments of two Scottish hospitals.
Casey, R.; Ludwig, S.; McCormick, M. C. (1987) Minor head trauma in children: an intervention to decrease functional morbidity. Pediatrics 80(2): 159-64	- Study does not contain an intervention relevant to this review protocol Study compared intervention to reduce functional morbidity after head trauma vs routine discharge instructions in children.

Study	Code [Reason]
de Koning, M. E., Scheenen, M. E., van der Horn, H. J. et al. (2017) Non-Hospitalized Patients with Mild Traumatic Brain Injury: The Forgotten Minority. Journal of Neurotrauma 34(1): 257-261	- Population not relevant to this review protocol Study describes injury and outcome characteristics of non-hospitalized mild TBI patients, and the possibility of predicting which of the non-hospitalised patients will return to the outpatient neurology clinic
de Kruijk, J. R., Leffers, P., Meerhoff, S. et al. (2002) Effectiveness of bed rest after mild traumatic brain injury: a randomised trial of no versus six days of bed rest. Journal of Neurology, Neurosurgery & Psychiatry 73(2): 167-72	- Study does not contain an intervention relevant to this review protocol Study compared bed rest vs no bed rest after head trauma.
De Maio, V. J., Joseph, D. O., Tibbo-Valeriote, H. et al. (2014) Variability in discharge instructions and activity restrictions for patients in a children's ED postconcussion. Pediatric Emergency Care 30(1): 20-5	- Study does not contain an intervention relevant to this review protocol study objective was to describe discharge instructions given to school-aged patients evaluated in a children's emergency department (ED) following concussion
Dias, M. S.; Carnevale, F.; Li, V. (1999) Immediate posttraumatic seizures: is routine hospitalization necessary?. Pediatric Neurosurgery 30(5): 232-8	- Population not relevant to this review protocol Study aimed to determine whether children with minor head injury and immediate post-traumatic seizures could be safely discharged from emergency room.
Dias, M. S., Lillis, K. A., Calvo, C. et al. (2004) Management of accidental minor head injuries in children: a prospective outcomes study. Journal of Neurosurgery 101(1suppl): 38-43	- Population not relevant to this review protocol Includes management of children with accidental minor head injuries with LOC/amnesia/vomiting/persistent lethargy.
Drexelius, N. (2006) Mild head injury: CT or observation?. Zeitschrift fur allgemeinmedizin 82(12): 529	- Full text paper not available
Fishe, J. N., Luberti, A. A., Master, C. L. et al. (2016) After-Hours Call Center Triage of Pediatric Head Injury: Outcomes After a Concussion Initiative. Pediatric Emergency Care 32(3): 149-53	- Study does not contain an intervention relevant to this review protocol Aim of the study is to characterise referral patterns and medical outcomes in children with head injury by an after of hours call centre.
Gupta, S., Kaafarani, H. M. A., Fagenholz, P. J. et al. (2020) Mild traumatic brain injuries with minor intracranial hemorrhage: Can they Be safely managed in the community? - A cohort study. International Journal Of Surgery 76: 88-92	- Population not relevant to this review protocol Patients with mild TBI and minor findings on head CT.

Study	Code [Reason]
Guzel, A., Hicdonmez, T., Temizoz, O. et al. (2009) Indications for brain computed tomography and hospital admission in pediatric patients with minor head injury: how much can we rely upon clinical findings?. Pediatric Neurosurgery 45(4): 262-70	- Study does not contain an intervention relevant to this review protocol Study aims to describe characteristics of patients with a minor head injury (MHI) who were admitted to a paediatric emergency unit and to identify the clinical signs and symptoms that most reliably predict the need for cranial computed tomography (CCT) and hospital admission following MHI.
Halbert, C. A., Cipolle, M. D., Fulda, G. J. et al. (2015) Admission to an observational unit improves length of stay for patients with mild traumatic brain injuries. American Surgeon 81(2): 178-81	- Population not relevant to this review protocol People with mild TBI with GCS greater than 14 to 15 and with or without a minor finding on CT scan. The minor CT scan findings included subcentimeter intraparenchymal or subdural hematoma.
Hartwell, J. L., Spalding, M. C., Fletcher, B. et al. (2015) You cannot go home: routine concussion evaluation is not enough. American Surgeon 81(4): 395-403	- No comparison group
Holsti, M., Kadish, H. A., Sill, B. L. et al. (2005) Pediatric closed head injuries treated in an observation unit. Pediatric Emergency Care 21(10): 639-44	- Study does not contain an intervention relevant to this review protocol Study aims to describe characteristics of patients with a closed head injury admitted to a paediatric observation unit and identify demographic, historical, clinical, and radiographic factors associated with the need for unplanned inpatient admission after observation unit management.
Holmes, J. F., Borgialli, D. A., Nadel, F. M. et al. (2011) Do children with blunt head trauma and normal cranial computed tomography scan results require hospitalization for neurologic observation?. Annals of Emergency Medicine 58(4): 315-22	-Planned secondary analysis of a prospective cohort study. Inappropriate population- people who underwent CT were at high risk of traumatic findings on CT. No protocol outcomes.
Hunter, F. and Choudhery, V. (2013) Towards evidence-based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 3: Management of paediatric minor head injuries: safe discharge?. Emergency medicine journal: EMJ 30(2): 166-7	- Review. Screened for relevant references.
Huynh, T., Jacobs, D. G., Dix, S. et al. (2006) Utility of neurosurgical consultation for mild traumatic brain injury. American Surgeon 72(12): 1162-5; discussion1166	- Population not relevant to this review protocol People with GCS 15 and abnormal head CT scan.

Study	Code [Reason]
Ingebrigtsen, T.; Romner, B.; Kock-Jensen, C. (2000) Scandinavian guidelines for initial management of minimal, mild, and moderate head injuries. The Scandinavian Neurotrauma Committee. The Journal of trauma 48(4): 760-6	- Review article but not a systematic review
Kempe, C. B.; Sullivan, K. A.; Edmed, S. L. (2013) CE the effect of varying diagnostic terminology within patient discharge information on expected mild traumatic brain injury outcome. Clinical Neuropsychologist 27(5): 762-78	- Study does not contain an intervention relevant to this review protocol Study aimed to determine if variation of diagnostic terminology in discharge information (concussion or mild TBI) would produce different expected symptoms and illness perceptions.
Leitner, L., El-Shabrawi, J. H., Bratschitsch, G. et al. (2021) Risk adapted diagnostics and hospitalization following mild traumatic brain injury. Archives of Orthopaedic & Trauma Surgery 141(4): 619-627	- Study does not contain an intervention relevant to this review protocol Study aims to determine risk factors predicting intracranial haemorrhage, progression and death in patients hospitalised with mild TBI
Lindholm, E. B., D'Cruz, R., Fajardo, R. et al. (2019) Admission of Pediatric Concussion Injury Patients: Is It Necessary?. Journal of Surgical Research 244: 107-110	- No comparison group
Luckhoff, C. and Starr, M. (2010) Minor head injuries in children - an approach to management. Australian Family Physician 39(5): 284-7	- Article
M, L. Wilson, Tenovuo, O., Mattila, V. M. et al. (2017) Pediatric TBI in Finland: An examination of hospital discharges (1998-2012). European Journal of Paediatric Neurology 21(2): 374-381	- Study does not contain an intervention relevant to this review protocol study aims to clarify the incidence, type and geographical presentation of paediatric TBI in Finland.
Mandera, M., Wencel, T., Bazowski, P. et al. (2000) How should we manage children after mild head injury?. Childs Nervous System 16(3): 156-60	- Study does not contain an intervention relevant to this review protocol Study aims to identify factors that might allow identification of patients at risk of subsequent deterioration in children with mild head injury.
Marincowitz, C., Lecky, F. E., Townend, W. et al. (2018) A protocol for the development of a prediction model in mild traumatic brain injury with CT scan abnormality: which patients are safe for discharge?. Diagnostic and Prognostic Research 2: 6	- Protocol Protocol for a retrospective case note review

Study	Code [Reason]
Marincowitz, C., Lecky, F. E., Townend, W. et al. (2018) The Risk of Deterioration in GCS13-15 Patients with Traumatic Brain Injury Identified by Computed Tomography Imaging: A Systematic Review and Meta-Analysis. Journal of Neurotrauma 35(5): 703-718	- Population not relevant to this review protocol Management of mild TBI patients with injuries identified by CT
Marincowitz, C., Lecky, F., Townend, W. et al. (2017) 4 The risk of deterioration in CT identified mild traumatic brain injury: a systematic review and meta-analysis. Emergency medicine journal: EMJ 34(12): A862-A863	- Study does not contain an intervention relevant to this review protocol Study aims to estimate the risk of death, neurosurgery and clinical deterioration in mild TBI identified by CT.
Mastrangelo, M. and Midulla, F. (2017) Minor Head Trauma in the Pediatric Emergency Department: Decision Making Nodes. Current Pediatric Review 13(2): 92-99	- Study does not contain an intervention relevant to this review protocol Clinical decision rules
Mitchell, K. A., Fallat, M. E., Raque, G. H. et al. (1994) Evaluation of minor head injury in children. Journal of Pediatric Surgery 29(7): 851-4	- Population not relevant to this review protocol Study aims to evaluate criteria for hospitalisation in children with head injury with GCS > 12 or more. Includes children with and without CT abnormalities. No comparison group.
Pozzato, I., Meares, S., Kifley, A. et al. (2020) Challenges in the acute identification of mild traumatic brain injuries: Results from an emergency department surveillance study. BMJ Open 10 (2)	- Study does not contain an intervention relevant to this review protocol Retrospective review to establish proportion of mild TBI diagnosis among people presenting to an ED.
Pruitt, P., Penn, J., Peak, D. et al. (2017) Identifying patients with mild traumatic intracranial hemorrhage at low risk of decompensation who are safe for ED observation. American Journal of Emergency Medicine 35(2): 255-259	- Population not relevant to this review protocol Patients with traumatic intracranial haemorrhage and mild traumatic brain injury.
Rai, B., McCartan, F., Kaninde, A. et al. (2018) Infants with head injuries-do all need hospital admission?. Irish Journal of Medical Science 187(1): 141-143	- No comparison group
Roberts, R. M.; Bunting, J.; Pertini, M. (2017) Factors that predict discharge recommendations following paediatric mild traumatic brain injury. Brain Injury 31(8): 1109-1115	- Study does not contain an intervention relevant to this review protocol Study investigates factors that predict discharge recommendations for children and adolescents who present to an Australian paediatric Emergency Department (ED) following a mild traumatic brain injury.

Study	Code [Reason]
Ros, S. P. and Ros, M. A. (1989) Should patients with normal cranial CT scans following minor head injury be hospitalized for observation?. Pediatric Emergency Care 5(4): 216-218	- No comparison group
Schaller, B., Evangelopoulos, D. S., Muller, C. et al. (2010) Do we really need 24-h observation for patients with minimal brain injury and small intracranial bleeding? The Bernese Trauma Unit Protocol. Emergency Medicine Journal 27(7): 537-9	 Population not relevant to this review protocol People with mild head injury and small intracranial bleeding. No comparison group
Schoonman, G. G.; Bakker, D. P.; Jellema, K. (2014) Low risk of late intracranial complications in mild traumatic brain injury patients using oral anticoagulation after an initial normal brain computed tomography scan: education instead of hospitalization. European Journal of Neurology 21(7): 1021-5	- Study does not contain an intervention relevant to this review protocol Study evaluates if use of oral anticoagulation is a risk factor for secondary deterioration in mild TBI patients after a normal CT scan.
Schutzman, S. A., Barnes, P., Duhaime, A. C. et al. (2001) Evaluation and management of children younger than two years old with apparently minor head trauma: proposed guidelines. Pediatrics 107(5): 983-93	- Article Guideline for management of children less than 2 years with minor head trauma.
Sharpe, S., Kool, B., Shepherd, M. et al. (2012) Mild traumatic brain injury: improving quality of care in the paediatric emergency department setting. Journal of Paediatrics & Child Health 48(2): 170-6	- Study design not relevant to this review protocol Clinical records
Sheedy, J., Geffen, G., Donnelly, J. et al. (2006) Emergency department assessment of mild traumatic brain injury and prediction of post-concussion symptoms at one month post injury. Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society 28(5): 755-72	- Study does not contain an intervention relevant to this review protocol Study investigates prediction of post-concussion symptoms using an ED assessment test.
Stopa, B. M., Amoroso, S., Ronfani, L. et al. (2019) Comparison of minor head trauma management in the emergency departments of a United States and Italian Children's hospital. Italian Journal of Pediatrics 45 (1)	- Inappropriate intervention and comparator study compares pediatric minor head trauma management between a US and Italian hospital.
Tavarez, M. M.; Atabaki, S. M.; Teach, S. J. (2012) Acute evaluation of pediatric patients	- Systematic screened for relevant references review on clinical decision rules.

Study	Code [Reason]
with minor traumatic brain injury. Current Opinion in Pediatrics 24(3): 307-13	
Tavender, E. J., Bosch, M., Green, S. et al. (2011) Quality and consistency of guidelines for the management of mild traumatic brain injury in the emergency department. Academic Emergency Medicine 18(8): 880-9	- Review article but not a systematic review Review of the recommendations and quality of evidence-based clinical practice guidelines for the emergency management of mild TBI.
Uccella, L., Zoia, C., Perlasca, F. et al. (2016) Mild Traumatic Brain Injury in Patients on Long- Term Anticoagulation Therapy: do They Really Need Repeated Head CT Scan?. World neurosurgery 93: 100-103	- Comparator in study does not match that specified in this review protocol anti-coagulated vs non-anticoagulated patients with mild TBI to assess risk of haemorrhage
Varner, C., Thompson, C., de Wit, K. et al. (2021) Predictors of persistent concussion symptoms in adults with acute mild traumatic brain injury presenting to the emergency department. CJEM Canadian Journal of Emergency Medical Care 23(3): 365-373	- Study does not contain an intervention relevant to this review protocol Study aims to identify risk factors associated with persistent concussion symptoms in adults with acute mild TBI.
Varner, C., Thompson, C., de Wit, K. et al. (2020) LO90: predictors of post-concussion syndrome in adults with acute mild traumatic brain injury presenting to the emergency department: a secondary analysis of a randomized controlled trialCanadian Association of Emergency Physicians (CAEP/ACMU) Conference, June 1-4, 2020, Ontario, Canada. CJEM: Canadian journal of emergency medicine 22(s1): 40	- Study does not contain an intervention relevant to this review protocol Predictors of post-concussion syndrome in adults with acute mild TBI in ED.
Verschoof, M. A., Zuurbier, C. C. M., de Beer, F. et al. (2018) Evaluation of the yield of 24-h close observation in patients with mild traumatic brain injury on anticoagulation therapy: a retrospective multicenter study and meta-analysis. Journal of Neurology 265(2): 315-321	- Population not relevant to this review protocol People with mild injury on anticoagulation therapy
Vikane, E., Hellstrom, T., Roe, C. et al. (2017) Multidisciplinary outpatient treatment in patients with mild traumatic brain injury: A randomised controlled intervention study. Brain Injury 31(4): 475-484	- Study does not contain an intervention relevant to this review protocol Study evaluates efficacy of a multi-disciplinary outpatient follow-up programme compared to a follow-up by a GP.
Wade, D. T., Crawford, S., Wenden, F. J. et al. (1997) Does routine follow up after head injury help? A randomised controlled trial. Journal of Neurology, Neurosurgery & Psychiatry 62(5): 478-84	- Study does not contain an intervention relevant to this review protocol Study compared routine follow-up vs follow-up 6 months after head injury

Study	Code [Reason]
Warren, D. and Kissoon, N. (1989) Usefulness of head injury instruction forms in home observation of mild head injuries. Pediatric emergency care 5(2): 83-85	- Study does not contain an intervention relevant to this review protocol Study evaluates the usefulness of head injury instruction forms
Yun, B. J., Borczuk, P., Wang, L. et al. (2018) Evaluation of a Low-risk Mild Traumatic Brain Injury and Intracranial Hemorrhage Emergency Department Observation Protocol. Academic Emergency Medicine 25(7): 769-775	 Population not relevant to this review protocol People with mild TBI and intracranial haemorrhage No comparison group

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Health Economic studies

- 7 Published health economic studies that met the inclusion criteria (relevant population,
- 8 comparators, economic study design, published 2006 or later and not from non-OECD
- 9 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.
- 11 None.