

Head Injury Tranexamic Acid

This literature search strategy was used for the following review:

- What is the clinical and cost effectiveness of tranexamic acid (TXA) for managing suspected or confirmed isolated traumatic intracranial bleeding pre-hospital and in hospital?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.{NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	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	

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) 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.	Tranexamic Acid/
27.	(tranexamic or txa or cyklokapron).ti,ab.
28.	or/26-27
29.	25 and 28

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 cranial or cerebral or skull) adj4 (injur* or trauma*)),ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial) 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.	(rat or rats or mouse or mice or rodent*).ti.

24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	tranexamic acid/
28.	(tranexamic or txa or cyklokapron).ti,ab.
29.	1197-18-8.rn.
30.	or/27-29
31.	26 and 30

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*)):ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	MeSH descriptor: [Tranexamic Acid] this term only
#13.	(tranexamic or txa or cyklokapron):ti,ab
#14.	#12 or #13
#15.	#11 AND #14

A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies
	Quality of Life 1946 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language

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

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/

33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))

#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Direct Transport 1.2

This literature search strategy was used for the following review:

- What is the clinical and cost effectiveness of pre-hospital strategies to convey people with head injury to a distant specialist neuroscience centre past a closer non-specialist unit?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 1: 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)

Medline (Ovid) search terms

1.	(trauma or (traumatic adj3 injur*)).ti,ab.
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2.	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/
3.	((skull or cranial) adj3 fracture*).ti,ab.
4.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).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.	emergency service, hospital/ or trauma centers/
27.	Neurosurgery/
28.	(neuroscien* or neurosurg* or neurol* or emergenc* or accident* or "A and E" or "A & E" or A&E or ICU).ti,ab.
29.	((special* or tertiary or critical care or intensive care or regional or district general or acute) adj2 (cent* or unit* or hospital* or facilit*)).ti,ab.
30.	(trauma adj2 (centre* or center* or network* or service*)).ti,ab.
31.	or/26-30
32.	"transportation of patients"/ or exp ambulances/ or ambulance diversion/
33.	ambulance*.ti,ab.
34.	(transport* or transfer* or bypass or by pass or direct).ti,ab.
35.	or/32-34
36.	triage/
37.	(triage* or overtriage* or triaging).ti,ab.
38.	((pre-hospital or prehospital) adj3 (protocol* or guideline* or strateg* or tool* or index* or indices or score* or scoring or scale* or model* or rule* or criteria or calculat*)).ti,ab.
39.	((clinical or decision*) adj4 (tool or strateg*)).ti,ab.
40.	Decision support techniques/

41.	or/36-40
42.	35 or 41
43.	25 and 31 and 42
44.	randomized controlled trial.pt.
45.	controlled clinical trial.pt.
46.	randomi#ed.ti,ab.
47.	placebo.ab.
48.	randomly.ti,ab.
49.	Clinical Trials as topic.sh.
50.	trial.ti.
51.	or/44-50
52.	Meta-Analysis/
53.	exp Meta-Analysis as Topic/
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.	Epidemiologic studies/
64.	Observational study/
65.	exp Cohort studies/
66.	(cohort adj (study or studies or analys* or data)).ti,ab.
67.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
68.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
69.	Controlled Before-After Studies/
70.	Historically Controlled Study/
71.	Interrupted Time Series Analysis/
72.	(before adj2 after adj2 (study or studies or data)).ti,ab.
73.	exp case control study/
74.	case control*.ti,ab.
75.	Cross-sectional studies/
76.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
77.	or/63-76
78.	43 and (51 or 62 or 77)

Embase (Ovid) search terms

1.	(trauma or (traumatic adj3 injur*)).ti,ab.
2.	head injury/
3.	exp brain injury/
4.	skull injury/ or exp skull fracture/
5.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
6.	((skull or cranial) adj3 fracture*).ti,ab.
7.	(trauma* and ((subdural or intracranial) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.
8.	or/1-7
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	(conference abstract or conference paper).pt.
13.	case report/ or case study/
14.	(letter or comment*).ti.
15.	or/9-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental Animal/
22.	animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice or rodent*).ti.
25.	or/17-24
26.	8 not 25
27.	limit 26 to English language
28.	exp hospital emergency service/
29.	neurosurgery/
30.	(neuroscien* or neurosurg* or neurol* or emergenc* or accident* or "A and E" or "A & E" or A&E or ICU).ti,ab.
31.	((special* or tertiary or critical care or intensive care or regional or district general or acute) adj2 (cent* or unit* or hospital* or facilit*)).ti,ab.
32.	(trauma adj2 (centre* or center* or network* or service*)).ti,ab.
33.	or/28-32
34.	patient transport/ or ambulance/ or emergency medical dispatch/
35.	"traffic and transport"/
36.	ambulance transportation/
37.	ambulance*.ti,ab.
38.	(transport* or transfer* or bypass or by pass or direct).ti,ab.
39.	or/34-38
40.	emergency health service/

41.	(triage* or overtriage* or triaging).ti,ab.
42.	((pre-hospital or prehospital) adj3 (protocol* or guideline* or strateg* or tool* or index* or indices or score* or scoring or scale* or model* or rule* or criteria or calculat*)).ti,ab.
43.	((clinical or decision*) adj4 (tool or strateg*)).ti,ab.
44.	exp clinical decision making/ or exp decision making/ or clinical decision rule/
45.	or/40-44
46.	39 or 45
47.	27 and 33 and 46
48.	random*.ti,ab.
49.	factorial*.ti,ab.
50.	(crossover* or cross over*).ti,ab.
51.	((doubl* or singl*) adj blind*).ti,ab.
52.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
53.	crossover procedure/
54.	single blind procedure/
55.	randomized controlled trial/
56.	double blind procedure/
57.	or/48-56
58.	systematic review/
59.	Meta-Analysis/
60.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
61.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
62.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
63.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
64.	(search* adj4 literature).ab.
65.	(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.
66.	cochrane.jw.
67.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
68.	or/58-67
69.	Clinical study/
70.	Observational study/
71.	Family study/
72.	Longitudinal study/
73.	Retrospective study/
74.	Prospective study/
75.	Cohort analysis/
76.	Follow-up/
77.	cohort*.ti,ab.
78.	76 and 77
79.	(cohort adj (study or studies or analys* or data)).ti,ab.
80.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.

81.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
82.	(before adj2 after adj2 (study or studies or data)).ti,ab.
83.	exp case control study/
84.	case control*.ti,ab.
85.	cross-sectional study/
86.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
87.	or/69-75,78-86
88.	47 and (57 or 68 or 87)

Cochrane Library (Wiley) search terms

#1.	(trauma or (traumatic near/3 injur*)):ti,ab
#2.	MeSH descriptor: [Craniocerebral Trauma] this term only
#3.	MeSH descriptor: [Brain Injuries] explode all trees
#4.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#5.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#6.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#7.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#8.	MeSH descriptor: [Skull Fractures] explode all trees
#9.	((skull or cranial) near/3 fracture*):ti,ab
#10.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#11.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*)):ti,ab
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13.	MeSH descriptor: [Emergency Service, Hospital] this term only
#14.	MeSH descriptor: [Trauma Centers] this term only
#15.	MeSH descriptor: [Neurosurgery] this term only
#16.	(neuroscien* or neurosurg* or neurol* or emergenc* or accident* or "A and E" or "A & E" or A&E or ICU):ti,ab
#17.	((special* or tertiary or critical care or intensive care or regional or district general or acute) near/2 (cent* or unit* or hospital* or facilit*)):ti,ab
#18.	(trauma near/2 (centre* or center* or network* or service*)):ti,ab
#19.	#13 or #14 or #15 or #16 or #17 or #18
#20.	MeSH descriptor: [Transportation of Patients] this term only
#21.	MeSH descriptor: [Ambulance Diversion] this term only
#22.	MeSH descriptor: [Ambulances] explode all trees
#23.	ambulance*:ti,ab
#24.	(transport* or transfer* or bypass or by pass or direct):ti,ab
#25.	#20 or #21 or #22 or #23 or #24
#26.	MeSH descriptor: [Triage] this term only
#27.	(triage* or overtriage* or triaging):ti,ab
#28.	((pre-hospital or prehospital) near/3 (protocol* or guideline* or strateg* or tool* or index* or indices or score* or scoring or scale* or model* or rule* or criteria or calculat*)):ti,ab
#29.	((clinical or decision*) near/4 (tool or strateg*)):ti,ab

#30.	MeSH descriptor: [Decision Support Techniques] this term only
#31.	#26 or #27 or #28 or #29 or #30
#32.	#25 or #31
#33.	#12 and #19 and #32

Epistemonikos search terms

1.	(advanced_title_en:(((advanced_title_en:(((trauma OR traumatic) AND (injury OR injuries)))) OR advanced_abstract_en:(((trauma OR traumatic) AND (injury OR injuries)))) OR (advanced_title_en:(((skull OR cranial) AND fracture*)) OR advanced_abstract_en:(((skull OR cranial) AND fracture*))) OR (advanced_title_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*))) OR advanced_abstract_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))) OR advanced_abstract_en:(((advanced_title_en:(((trauma OR traumatic) AND (injury OR injuries))) OR advanced_abstract_en:(((trauma OR traumatic) AND (injury OR injuries)))) OR (advanced_title_en:(((skull OR cranial) AND fracture*)) OR advanced_abstract_en:(((skull OR cranial) AND fracture*))) OR (advanced_title_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*))) OR advanced_abstract_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))))) AND (advanced_title_en:((neuroscien* OR neurosurg* OR neurol* OR emergenc* OR accident* OR "A AND E" OR "A & E" OR A&E OR ICU)) OR advanced_abstract_en:((neuroscien* OR neurosurg* OR neurol* OR emergenc* OR accident* OR "A AND E" OR "A & E" OR A&E OR ICU)) OR (advanced_title_en:(((special* OR tertiary OR critical care OR intensive care OR regional OR district general OR acute) adj2 (cent* OR unit* OR hospital* OR facilit*))) OR advanced_abstract_en:(((special* OR tertiary OR critical care OR intensive care OR regional OR district general OR acute) adj2 (cent* OR unit* OR hospital* OR facilit*)))) OR (advanced_title_en:((trauma AND (centre* OR center* OR network* OR service*))) OR advanced_abstract_en:((trauma AND (centre* OR center* OR network* OR service*)))) AND (advanced_title_en:((ambulance* OR transport* OR transfer* OR bypass OR by pass OR direct OR triage* OR overtriage* OR triaging)) OR advanced_abstract_en:((ambulance* OR transport* OR transfer* OR bypass OR by pass OR direct OR triage* OR overtriage* OR triaging))) OR (advanced_title_en:(((pre-hospital OR prehospital) AND (protocol* OR guideline* OR strateg* OR tool* OR index* OR indices OR score* OR scoring OR scale* OR model* OR rule* OR criteria OR calculat*))) OR advanced_abstract_en:(((pre-hospital OR prehospital) AND (protocol* OR guideline* OR strateg* OR tool* OR index* OR indices OR score* OR scoring OR scale* OR model* OR rule* OR criteria OR calculat*)))) OR (advanced_title_en:(((clinical OR decision*) AND (tool OR strateg* OR rule*))) OR advanced_abstract_en:(((clinical OR decision*) AND (tool OR strateg*))))))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies

Database	Dates searched	Search filters and limits applied
	Quality of Life 1946 – 22 June 2022	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
	Quality of Life 1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31 st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31 st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24

26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Direct Access Imaging 1.3

This literature search strategy was used for the following review:

- What is the clinical and cost effectiveness of providing direct access from the community to imaging?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.{NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 1: 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)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) 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.	tomography/
27.	magnetic resonance imaging/ or exp diffusion magnetic resonance imaging/ or echo-planar imaging/ or fluorine-19 magnetic resonance imaging/ or magnetic resonance angiography/ or magnetic resonance imaging, cine/ or multiparametric magnetic resonance imaging/
28.	exp tomography, emission-computed/
29.	exp tomography, x-ray/
30.	(compute* adj2 tomograph*).ti,ab.
31.	(CT or CAT or PET or SPECT).ti,ab.
32.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph*)).ti,ab.
33.	MRI.ti,ab.
34.	((echo-planar or echoplanar or EPI) adj2 (imag* or sequenc*)).ti,ab.
35.	or/26-34
36.	25 and 35
37.	randomized controlled trial.pt.
38.	controlled clinical trial.pt.
39.	randomi#ed.ti,ab.

40.	placebo.ab.
41.	randomly.ti,ab.
42.	Clinical Trials as topic.sh.
43.	trial.ti.
44.	or/37-43
45.	Meta-Analysis/
46.	exp Meta-Analysis as Topic/
47.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
48.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
49.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
50.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
51.	(search* adj4 literature).ab.
52.	(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.
53.	cochrane.jw.
54.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
55.	or/45-54
56.	Epidemiologic studies/
57.	Observational study/
58.	exp Cohort studies/
59.	(cohort adj (study or studies or analys* or data)).ti,ab.
60.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
61.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
62.	Controlled Before-After Studies/
63.	Historically Controlled Study/
64.	Interrupted Time Series Analysis/
65.	(before adj2 after adj2 (study or studies or data)).ti,ab.
66.	exp case control study/
67.	case control*.ti,ab.
68.	Cross-sectional studies/
69.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
70.	or/56-70
71.	36 and (44 or 55 or 70)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.

6.	(trauma* and ((subdural or intracranial) 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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to english language
27.	tomography/
28.	brain tomography/
29.	exp computer assisted tomography/
30.	exp emission tomography/
31.	exp x-ray tomography/
32.	exp nuclear magnetic resonance imaging/
33.	(compute* adj2 tomograph*).ti,ab.
34.	(CT or CAT or PET or SPECT).ti,ab.
35.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph*).ti,ab.
36.	MRI.ti,ab.
37.	((echo-planar or echoplanar or EPI) adj2 (imag* or sequenc*).ti,ab.
38.	or/27-37
39.	26 and 38
40.	random*.ti,ab.
41.	factorial*.ti,ab.
42.	(crossover* or cross over*).ti,ab.
43.	((doubl* or singl*) adj blind*).ti,ab.
44.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
45.	crossover procedure/
46.	single blind procedure/
47.	randomized controlled trial/

48.	double blind procedure/
49.	or/40-48
50.	systematic review/
51.	Meta-Analysis/
52.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
53.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
54.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
55.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
56.	(search* adj4 literature).ab.
57.	(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.
58.	cochrane.jw.
59.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
60.	or/50-59
61.	Clinical study/
62.	Observational study/
63.	Family study/
64.	Longitudinal study/
65.	Retrospective study/
66.	Prospective study/
67.	Cohort analysis/
68.	Follow-up/
69.	cohort*.ti,ab.
70.	68 and 69
71.	(cohort adj (study or studies or analys* or data)).ti,ab.
72.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
73.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
74.	(before adj2 after adj2 (study or studies or data)).ti,ab.
75.	exp case control study/
76.	case control*.ti,ab.
77.	cross-sectional study/
78.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
79.	or/61-67,70-78
80.	39 and (49 or 60 or 79)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only

#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*)):ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	MeSH descriptor: [Tomography] this term only
#13.	MeSH descriptor: [Tomography, Emission-Computed] explode all trees
#14.	MeSH descriptor: [Tomography, X-Ray] explode all trees
#15.	MeSH descriptor: [Magnetic Resonance Imaging] this term only
#16.	MeSH descriptor: [Diffusion Magnetic Resonance Imaging] explode all trees
#17.	MeSH descriptor: [Echo-Planar Imaging] this term only
#18.	MeSH descriptor: [Fluorine-19 Magnetic Resonance Imaging] this term only
#19.	MeSH descriptor: [Magnetic Resonance Angiography] this term only
#20.	MeSH descriptor: [Magnetic Resonance Imaging, Cine] this term only
#21.	MeSH descriptor: [Multiparametric Magnetic Resonance Imaging] this term only
#22.	(compute* near/2 tomograph*):ti,ab
#23.	(CT or CAT or PET or SPECT):ti,ab
#24.	((MR or magnetic resonance or NMR) near/2 (imag* or tomograph* or angiograph*)):ti,ab
#25.	MRI:ti,ab
#26.	((echo-planar or echoplanar or EPI) near/2 (imag* or sequenc*)):ti,ab
#27.	#12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
#28.	#11 and #27

Epistemonikos search terms

1.	(advanced_title_en:(((skull OR cranial) AND fracture*)) OR advanced_abstract_en:(((skull OR cranial) AND fracture*))) OR (advanced_title_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*))) OR advanced_abstract_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))) AND (advanced_title_en:(tomograph* OR magnetic resonance OR echoplanar OR echo-planar OR neuroimag* OR MRI OR CT OR CAT OR PET OR SPECT OR EPI)) OR advanced_abstract_en:(tomograph* OR magnetic resonance OR echoplanar OR echo-planar OR neuroimag* OR MRI OR CT OR CAT OR PET OR SPECT OR EPI))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

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

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/42-61
63.	25 and (42 or 62)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Clinical Decision Rules – Indications for Imaging Diagnostic 2.1A

This literature search strategy was used for the following review:

- What are the indications for selecting adults, young people, children and babies with head injury for CT or MRI head scan?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Diagnostic tests studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	Diagnostic tests 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)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) 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.	(NEXUS or NOC or CHIP or New Orleans criteria or CHALICE or PECARN).ti,ab.
27.	((Canadian or Scandinavian) adj2 (assess* or rule*)).ti,ab.
28.	or/26-27
29.	25 and 28
30.	tomography/ or exp tomography, emission-computed/ or exp tomography, x-ray/
31.	(compute* adj2 tomograph*).ti,ab.
32.	magnetic resonance imaging/
33.	MRI.ti,ab.
34.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph*)).ti,ab.
35.	(CT or CAT or PET or SPECT).ti,ab.
36.	or/30-35
37.	predict.ti.
38.	(validat* or rule*).ti,ab.
39.	(predict* and (outcome* or risk* or model*)).ti,ab.
40.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
41.	decision*.ti,ab. and Logistic models/
42.	(decision* and (model* or clinical*)).ti,ab.

43.	(prognostic and (history or variable\$ or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
44.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
45.	ROC curve/
46.	or/37-45
47.	triage/
48.	(triage* or overtriage* or triaging).ti,ab.
49.	(predict* adj4 (tool* or index* or indices or score* or scoring or scale* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.
50.	(risk* adj4 (tool* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.
51.	(prognos* adj4 (tool* or index* or indices or scale* or system* or algorithm* or stratif* or calculat*)).ti,ab.
52.	((clinical or decision*) adj4 (tool or strateg*)).ti,ab.
53.	Decision support techniques/
54.	or/47-53
55.	exp "sensitivity and specificity"/
56.	(sensitivity or specificity).ti,ab.
57.	((pre test or pretest or post test) adj probability).ti,ab.
58.	(predictive value* or PPV or NPV).ti,ab.
59.	likelihood ratio*.ti,ab.
60.	likelihood function/
61.	((area under adj4 curve) or AUC).ti,ab.
62.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
63.	(diagnos* adj2 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
64.	gold standard.ab.
65.	exp Diagnostic errors/
66.	(false positiv* or false negativ*).ti,ab.
67.	Diagnosis, Differential/
68.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness or precision or validat* or validity or differential or error*)).ti,ab.
69.	or/55-68
70.	46 or 54 or 69
71.	25 and 36 and 70
72.	29 or 71

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.

6.	(trauma* and ((subdural or intracranial) 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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	(NEXUS or NOC or CHIP or New Orleans criteria or CHALICE or PECARN).ti,ab.
28.	((Canadian or Scandinavian) adj2 (assess* or rule*)).ti,ab.
29.	or/27-28
30.	26 and 29
31.	tomography/
32.	brain tomography/
33.	exp computer assisted tomography/
34.	exp emission tomography/
35.	exp x-ray tomography/
36.	(compute* adj2 tomograph*).ti,ab.
37.	nuclear magnetic resonance imaging/
38.	MRI.ti,ab.
39.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph*)).ti,ab.
40.	(CT or CAT or PET or SPECT).ti,ab.
41.	or/31-40
42.	predict.ti.
43.	(validat* or rule*).ti,ab.
44.	(predict* and (outcome* or risk* or model*)).ti,ab.
45.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.

46.	decision*.ti,ab. and Statistical model/
47.	(decision* and (model* or clinical*)).ti,ab.
48.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
49.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
50.	Receiver operating characteristic/
51.	or/42-50
52.	emergency health service/
53.	(triage* or overtriage* or triaging).ti,ab.
54.	(predict* adj4 (tool* or index* or indices or score* or scoring or scale* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.
55.	(risk* adj4 (tool* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.
56.	(prognos* adj4 (tool* or index* or indices or scale* or system* or algorithm* or stratif* or calculat*)).ti,ab.
57.	((clinical or decision*) adj4 (tool or strateg*)).ti,ab.
58.	exp decision support system/
59.	or/52-58
60.	exp "sensitivity and specificity"/
61.	(sensitivity or specificity).ti,ab.
62.	((pre test or pretest or post test) adj probability).ti,ab.
63.	(predictive value* or PPV or NPV).ti,ab.
64.	likelihood ratio*.ti,ab.
65.	((area under adj4 curve) or AUC).ti,ab.
66.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
67.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
68.	diagnostic accuracy/
69.	diagnostic test accuracy study/
70.	gold standard.ab.
71.	exp diagnostic error/
72.	(false positiv* or false negativ*).ti,ab.
73.	differential diagnosis/
74.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness or precision or validat* or validity or differential or error*)).ti,ab.
75.	or/60-74
76.	51 or 59 or 75
77.	26 and 41 and 76
78.	30 or 77

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees

#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*))) :ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	MeSH descriptor: [Tomography] this term only
#13.	MeSH descriptor: [Tomography, Emission-Computed] explode all trees
#14.	MeSH descriptor: [Tomography, X-Ray] explode all trees
#15.	(compute* NEAR/2 tomograph*):ti,ab
#16.	MeSH descriptor: [Magnetic Resonance Imaging] this term only
#17.	MRI:ti,ab
#18.	((MR or magnetic resonance or NMR) NEAR/2 (imag* or tomograph*)):ti,ab
#19.	(CT or CAT or PET or SPECT):ti,ab
#20.	#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21.	#11 AND #20

Epistemonikos search terms

1.	(advanced_title_en:(((skull OR cranial) AND fracture*)) OR advanced_abstract_en:(((skull OR cranial) AND fracture*))) OR (advanced_title_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*))) OR advanced_abstract_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))) AND (advanced_title_en:(tomograph* OR magnetic resonance OR neuroimag* OR MRI OR CT OR CAT OR PET OR SPECT)) OR advanced_abstract_en:(tomograph* OR magnetic resonance OR neuroimag* OR MRI OR CT OR CAT OR PET OR SPECT))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies

Database	Dates searched	Search filters and limits applied
	Quality of Life 1946 – 22 June 2022	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
	Quality of Life 1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31 st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31 st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury – Indications for Imaging in sub groups 2.1B

This literature search strategy was used for the following review:

- What are the indications for selecting adults, young people, children and infants with head injury for CT or MRI head scan in a sub-group including;
 - people on anticoagulant or antiplatelet therapy, including those with no history of amnesia or loss of consciousness
 - people with liver or coagulopathy disorders
 - people with pre-injury cognitive impairment sustaining injury through low level falls
 - people sustaining recurrent head injuries through sport
 - people presenting more than 24 hours after injury?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	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	

Database	Dates searched	Search filter used
Epistemonikos (The Epistemonikos Foundation)	Inception to 22 June 2022	Exclusions (Cochrane reviews)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) 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.	tomography/ or exp tomography, emission-computed/ or exp tomography, x-ray/
27.	(compute* adj2 tomograph*).ti,ab.
28.	magnetic resonance imaging/
29.	MRI.ti,ab.
30.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph*)).ti,ab.
31.	(CT or CAT or PET or SPECT).ti,ab.
32.	or/26-31
33.	25 and 32
34.	Epidemiologic studies/

35.	Observational study/
36.	exp Cohort studies/
37.	(cohort adj (study or studies or analys* or data)).ti,ab.
38.	((follow up or observational or uncontrolled or non random#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
39.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
40.	Controlled Before-After Studies/
41.	Historically Controlled Study/
42.	Interrupted Time Series Analysis/
43.	(before adj2 after adj2 (study or studies or data)).ti,ab.
44.	Cross-sectional studies/
45.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
46.	or/34-45
47.	Meta-Analysis/
48.	exp Meta-Analysis as Topic/
49.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
50.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
51.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
52.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
53.	(search* adj4 literature).ab.
54.	(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.
55.	cochrane.jw.
56.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
57.	or/47-56
58.	46 or 57
59.	33 and 58

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial) 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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to english language
27.	*tomography/
28.	*brain tomography/
29.	exp *computer assisted tomography/
30.	exp *emission tomography/
31.	exp *x-ray tomography/
32.	(compute* adj2 tomograph*).ti,ab.
33.	*nuclear magnetic resonance imaging/
34.	MRI.ti,ab.
35.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph*)).ti,ab.
36.	(CT or CAT or PET or SPECT).ti,ab.
37.	or/27-36
38.	26 and 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.	cross-sectional study/
54.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
55.	or/39-45,48-54
56.	systematic review/
57.	Meta-Analysis/
58.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
59.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
60.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
61.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
62.	(search* adj4 literature).ab.
63.	(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.
64.	cochrane.jw.
65.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
66.	or/56-65
67.	55 or 66
68.	38 and 67

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*)):ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	MeSH descriptor: [Tomography] this term only
#13.	MeSH descriptor: [Tomography, Emission-Computed] explode all trees
#14.	MeSH descriptor: [Tomography, X-Ray] explode all trees
#15.	(compute* NEAR/2 tomograph*):ti,ab
#16.	MeSH descriptor: [Magnetic Resonance Imaging] this term only
#17.	MRI:ti,ab
#18.	((MR or magnetic resonance or NMR) NEAR/2 (imag* or tomograph*)):ti,ab
#19.	(CT or CAT or PET or SPECT):ti,ab
#20.	#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21.	#11 AND #20

Epistemonikos search terms

1.	(advanced_title_en:(((skull OR cranial) AND fracture*)) OR advanced_abstract_en:(((skull OR cranial) AND fracture*))) OR (advanced_title_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*))) OR advanced_abstract_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))) AND (advanced_title_en:(tomograph* OR magnetic resonance OR neuroimag* OR MRI OR CT OR CAT OR PET OR SPECT)) OR advanced_abstract_en:(tomograph* OR magnetic resonance OR neuroimag* OR MRI OR CT OR CAT OR PET OR SPECT))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

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

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title]) AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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])

Head Injury Biomarkers 2.2A/B

This literature search strategy was used for the following review:

- What is the prognostic accuracy of brain injury biomarkers and/or MRI for predicting post-concussion syndrome?
- What is the clinical and cost effectiveness of biomarkers and/or MRI when each is followed by the appropriate treatment for post-concussion syndrome to improve patient outcomes?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.{NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 1: 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	

Database	Dates searched	Search filter used
Epistemonikos (The Epistemonikos Foundation)	Inception to 22 June 2022	Exclusions (Cochrane reviews)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.
5.	or/1-4
6.	(concuss* or postconcuss* or PCSS).ti,ab.
7.	5 or 6
8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice or rodent*).ti.
25.	or/18-24
26.	7 not 25
27.	limit 26 to English language
28.	exp Biomarkers/
29.	exp S100 Proteins/
30.	Glial Fibrillary Acidic Protein/
31.	Phosphopyruvate Hydratase/
32.	Ubiquitin Thiolesterase/
33.	exp MicroRNAs/
34.	Brain-Derived Neurotrophic Factor/

35.	Neurofilament Proteins/
36.	Spectrin/
37.	Myelin Basic Protein/
38.	exp Extracellular Vesicles/
39.	tau Proteins/
40.	(Ubiquitin Thiolesterase* or "Ubiquitin C-terminal hydrolase*" or "Ubiquitin C-Terminal Esterase*" or "Ubiquitin Carboxy-Terminal Hydrolase*" or "Ubiquitin Carboxy-Terminal Esterase*" or uch-l1 or UCHL1).ti,ab.
41.	(S100* or GFAP or "glial fibrillary acid* protein*" or "brain-derived neurotrophic factor*" or "brain-derived nerve growth factor*" or BDNF or spectrin* or tau or proteomic* or microRNA* or miRNA* or micro-rna*).ti,ab.
42.	((muscle or nervous or neuron* or alpha or beta or gamma) adj3 enolase*).ti,ab.
43.	(Phosphopyruvate Hydratase* or 2-phosphoglycerate* or 2-phospho-D-glycerate* or NSE).ti,ab.
44.	((neurofilament* adj3 (protein* or chain* or polypeptide*)) or NF-L or NF-H).ti,ab.
45.	((myelin basic or nerve tissue* or golli* or hog* or mbp*) adj2 protein*).ti,ab.
46.	((((extracellular or secretory) adj vesicle*) or exovesicle* or apoptotic bod* or exosome* or endosome* or ectosome* or microvesicle* or ((membrane or cell-derived) adj microparticle*)).ti,ab.
47.	biomarker*.ti,ab,kf.
48.	marker*.ti,ab.
49.	or/28-48
50.	exp magnetic resonance imaging/
51.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph* or functional or advanced or structural)).ti,ab.
52.	((echo-planar or echoplanar or EPI) adj2 (imag* or sequenc*)).ti,ab.
53.	(diffusion adj3 imag*).ti,ab.
54.	neuroimag*.ti,ab.
55.	MRI.ti,ab.
56.	or/50-55
57.	49 or 56
58.	27 and 57
59.	randomized controlled trial.pt.
60.	controlled clinical trial.pt.
61.	randomi#ed.ti,ab.
62.	placebo.ab.
63.	randomly.ti,ab.
64.	Clinical Trials as topic.sh.
65.	trial.ti.
66.	or/59-65
67.	Meta-Analysis/
68.	exp Meta-Analysis as Topic/
69.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.

70.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
71.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
72.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
73.	(search* adj4 literature).ab.
74.	(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.
75.	cochrane.jw.
76.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
77.	or/67-76
78.	Epidemiologic studies/
79.	Observational study/
80.	exp Cohort studies/
81.	(cohort adj (study or studies or analys* or data)).ti,ab.
82.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
83.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
84.	Controlled Before-After Studies/
85.	Historically Controlled Study/
86.	Interrupted Time Series Analysis/
87.	(before adj2 after adj2 (study or studies or data)).ti,ab.
88.	exp case control study/
89.	case control*.ti,ab.
90.	Cross-sectional studies/
91.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
92.	or/78-91
93.	predict.ti.
94.	(validat* or rule*).ti,ab.
95.	(predict* and (outcome* or risk* or model*)).ti,ab.
96.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
97.	decision*.ti,ab. and Logistic models/
98.	(decision* and (model* or clinical*)).ti,ab.
99.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
100.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
101.	ROC curve/
102.	Or/93-101
103.	58 and (66 or 77 or 92 or 102)

Embase (Ovid) search terms

1.	head injury/
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2.	exp brain injury/
3.	skull injury/ or exp skull fracture/
4.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.
7.	or/1-6
8.	(concuss* or postconcuss* or PCSS).ti,ab.
9.	or/7-8
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	(conference abstract or conference paper).pt.
14.	case report/ or case study/
15.	(letter or comment*).ti.
16.	or/10-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animal/ not human/
20.	nonhuman/
21.	exp Animal Experiment/
22.	exp Experimental Animal/
23.	animal model/
24.	exp Rodent/
25.	(rat or rats or mouse or mice or rodent*).ti.
26.	or/18-25
27.	9 not 26
28.	limit 27 to English language
29.	*biological marker/
30.	*protein S 100/
31.	*glial fibrillary acidic protein/
32.	*enolase/
33.	*ubiquitin thiolesterase/
34.	exp *microRNA/
35.	*brain derived neurotrophic factor/
36.	*neurofilament protein/
37.	*spectrin/
38.	*myelin basic protein/
39.	*exosome/
40.	*tau protein/

41.	(Ubiquitin Thiolesterase* or "Ubiquitin C-terminal hydrolase*" or "Ubiquitin C-Terminal Esterase*" or "Ubiquitin Carboxy-Terminal Hydrolase*" or "Ubiquitin Carboxy-Terminal Esterase*" or uch-l1 or UCHL1).ti,ab.
42.	(S100* or GFAP or "glial fibrillary acid* protein*" or "brain-derived neurotrophic factor*" or "brain-derived nerve growth factor*" or BDNF or spectrin* or tau or proteomic* or microRNA* or miRNA* or micro-rna*).ti,ab.
43.	((muscle or nervous or neuron* or alpha or beta or gamma) adj3 enolase*).ti,ab.
44.	(Phosphopyruvate Hydratase* or 2-phosphoglycerate* or 2-phospho-D-glycerate* or NSE).ti,ab.
45.	((neurofilament* adj3 (protein* or chain* or polypeptide*)) or NF-L or NF-H).ti,ab.
46.	((myelin basic or nerve tissue* or golli* or hog* or mbp*) adj2 protein*).ti,ab.
47.	((((extracellular or secretory) adj vesicle*) or exovesicle* or apoptotic bod* or exosome* or endosome* or ectosome* or microvesicle* or ((membrane or cell-derived) adj microparticle*)).ti,ab.
48.	biomarker*.ti,ab,kw.
49.	marker*.ti,ab.
50.	or/29-49
51.	exp *nuclear magnetic resonance imaging/
52.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph* or functional or advanced or structural)).ti,ab.
53.	((echo-planar or echoplanar or EPI) adj2 (imag* or sequenc*)).ti,ab.
54.	(diffusion adj3 imag*).ti,ab.
55.	neuroimag*.ti,ab.
56.	MRI.ti,ab.
57.	or/51-56
58.	50 or 57
59.	28 and 58
60.	random*.ti,ab.
61.	factorial*.ti,ab.
62.	(crossover* or cross over*).ti,ab.
63.	((doubl* or singl*) adj blind*).ti,ab.
64.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
65.	crossover procedure/
66.	single blind procedure/
67.	randomized controlled trial/
68.	double blind procedure/
69.	or/60-68
70.	systematic review/
71.	Meta-Analysis/
72.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
73.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
74.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.

75.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
76.	(search* adj4 literature).ab.
77.	(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.
78.	cochrane.jw.
79.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
80.	or/70-79
81.	Clinical study/
82.	Observational study/
83.	Family study/
84.	Longitudinal study/
85.	Retrospective study/
86.	Prospective study/
87.	Cohort analysis/
88.	Follow-up/
89.	cohort*.ti,ab.
90.	88 and 89
91.	(cohort adj (study or studies or analys* or data)).ti,ab.
92.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
93.	((longitudinal or retrospective or prospective ((cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
94.	(before adj2 after adj2 (study or studies or data)).ti,ab.
95.	exp case control study/
96.	case control*.ti,ab.
97.	cross-sectional study/
98.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
99.	or/81-87,90-98
100.	predict.ti.
101.	(validat* or rule*).ti,ab.
102.	(predict* and (outcome* or risk* or model*)).ti,ab.
103.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
104.	decision*.ti,ab. and Statistical model/
105.	(decision* and (model* or clinical*)).ti,ab.
106.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
107.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
108.	Receiver operating characteristic/
109.	Or/100-108
110.	59 and (69 or 80 or 99 or 109)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*))) :ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	(concuss* or postconcuss* or PCSS):ti,ab
#13.	#11 or #12
#14.	MeSH descriptor: [Biomarkers] explode all trees
#15.	MeSH descriptor: [S100 Proteins] explode all trees
#16.	MeSH descriptor: [Glial Fibrillary Acidic Protein] this term only
#17.	MeSH descriptor: [Phosphopyruvate Hydratase] this term only
#18.	MeSH descriptor: [Ubiquitin Thiolesterase] this term only
#19.	MeSH descriptor: [MicroRNAs] explode all trees
#20.	MeSH descriptor: [Brain-Derived Neurotrophic Factor] this term only
#21.	MeSH descriptor: [Neurofilament Proteins] this term only
#22.	MeSH descriptor: [Spectrin] this term only
#23.	MeSH descriptor: [Myelin Basic Protein] this term only
#24.	MeSH descriptor: [Extracellular Vesicles] explode all trees
#25.	MeSH descriptor: [tau Proteins] this term only
#26.	(Ubiquitin Thiolesterase* or "Ubiquitin C-terminal hydrolase*" or "Ubiquitin C-Terminal Esterase*" or "Ubiquitin Carboxy-Terminal Hydrolase*" or "Ubiquitin Carboxy-Terminal Esterase*" or uch-l1 or UCHL1):ti,ab
#27.	(S100* or GFAP or "glial fibrillary acid* protein*" or "brain-derived neurotrophic factor*" or "brain-derived nerve growth factor*" or BDNF or spectrin* or tau or proteomic* or microRNA* or miRNA* or micro-rna*):ti,ab
#28.	((muscle or nervous or neuron* or alpha or beta or gamma) near/3 enolase*):ti,ab
#29.	(Phosphopyruvate Hydratase* or 2phosphoglycerate* or 2phospho-D-glycerate* or NSE):ti,ab
#30.	((neurofilament* near/3 (protein* or chain* or polypeptide*)) or NF-L or NF-H):ti,ab
#31.	((myelin basic or nerve tissue* or golli* or hog* or mbp*) near/2 protein*):ti,ab
#32.	((((extracellular or secretory) near vesicle*) or exovesicle* or apoptotic bod* or exosome* or endosome* or ectosome* or microvesicle* or ((membrane or cell-derived) near microparticle*)):ti,ab
#33.	biomarker*:ti,ab,kw
#34.	marker*:ti,ab

#35.	#14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34
#36.	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#37.	((MR or magnetic resonance or NMR) near/2 (imag* or tomograph* or angiograph* or functional or advanced or structural)):ti,ab
#38.	((echo-planar or echoplanar or EPI) near/2 (imag* or sequenc*)):ti,ab
#39.	(diffusion near/3 imag*):ti,ab
#40.	neuroimag*:ti,ab
#41.	MRI:ti,ab
#42.	#36 or #37 or #38 or #39 or #40 or #41
#43.	#35 or #42
#44.	#13 and #43

Epistemonikos search terms

1.	(advanced_title_en:(((trauma OR traumatic) AND (injury OR injuries))) OR advanced_abstract_en:(((trauma OR traumatic) AND (injury OR injuries)))) OR (advanced_title_en:(((skull OR cranial) AND fracture*)) OR advanced_abstract_en:(((skull OR cranial) AND fracture*))) OR (advanced_title_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*))) OR advanced_abstract_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))) OR (advanced_title_en:(concuss* OR PCSS OR post-concuss*)) OR advanced_abstract_en:(concuss* OR PCSS OR post-concuss*)) AND (advanced_title_en:(biomarker* OR marker*)) OR advanced_abstract_en:(biomarker* OR marker*)) OR (advanced_title_en:(S100* OR GFAP OR "glial fibrillary acid* protein*" OR "brain-derived neurotrophic factor*" OR "brain-derived nerve growth factor*" OR BDNF OR spectrin* OR tau OR proteomic* OR microRNA* OR miRNA* OR micro-rna*)) OR advanced_abstract_en:(S100* OR GFAP OR "glial fibrillary acid* protein*" OR "brain-derived neurotrophic factor*" OR "brain-derived nerve growth factor*" OR BDNF OR spectrin* OR tau OR proteomic* OR microRNA* OR miRNA* OR micro-rna*)) OR (advanced_title_en:(Ubiquitin Thiolesterase* OR "Ubiquitin C-terminal hydrolase*" OR "Ubiquitin C-Terminal Esterase*" OR "Ubiquitin Carboxy-Terminal Hydrolase*" OR "Ubiquitin Carboxy-Terminal Esterase*" OR uch-11 OR UCHL1)) OR advanced_abstract_en:(Ubiquitin Thiolesterase* OR "Ubiquitin C-terminal hydrolase*" OR "Ubiquitin C-Terminal Esterase*" OR "Ubiquitin Carboxy-Terminal Hydrolase*" OR "Ubiquitin Carboxy-Terminal Esterase*" OR uch-11 OR UCHL1))) OR (advanced_title_en:(enolase* OR Phosphopyruvate Hydratase* OR 2-phosphoglycerate* OR 2-phospho-D-glycerate* OR NSE)) OR advanced_abstract_en:(enolase* OR Phosphopyruvate Hydratase* OR 2-phosphoglycerate* OR 2-phospho-D-glycerate* OR NSE))) OR (advanced_title_en:(neurofilament protein* OR myelin basic protein* OR extracellular vesicle* OR exovesicle* OR apoptotic bod* OR exosome* OR endosome* OR ectosome* OR microvesicle* OR cell-derived microparticle*)) OR advanced_abstract_en:(neurofilament protein* OR myelin basic protein* OR extracellular vesicle* OR exovesicle* OR apoptotic bod* OR exosome* OR endosome* OR ectosome* OR microvesicle* OR cell-derived microparticle*)) OR (advanced_title_en:(tomograph* OR magnetic resonance OR neuroimag* OR MRI Or echoplanar* OR diffusion tensor imag* OR diffusion weight* imag*)) OR advanced_abstract_en:(tomograph* OR magnetic resonance OR neuroimag* OR MRI Or echoplanar* OR diffusion tensor imag* OR diffusion weight* imag*))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

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

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	((skull or cranial) adj3 fracture*)
#9.	((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*)))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))) [Title]) AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Biomarkers 2.3A/B

This literature search strategy was used for the following review:

- What is the diagnostic accuracy of brain injury biomarkers for predicting acute post-brain injury complications?
- What is the clinical and cost effectiveness of biomarkers when followed by the appropriate treatment for acute post-brain injury complications to improve patient outcomes?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.{NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 1: 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 Diagnostic tests 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 Diagnostic tests 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	

Database	Dates searched	Search filter used
Epistemonikos (The Epistemonikos Foundation)	Inception to 22 June 2022	Exclusions (Cochrane reviews)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) 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.	exp Biomarkers/
27.	exp S100 Proteins/
28.	Glial Fibrillary Acidic Protein/
29.	Phosphopyruvate Hydratase/
30.	Ubiquitin Thiolesterase/
31.	exp MicroRNAs/
32.	Brain-Derived Neurotrophic Factor/
33.	Neurofilament Proteins/
34.	Spectrin/

35.	Myelin Basic Protein/
36.	exp Extracellular Vesicles/
37.	tau Proteins/
38.	(Ubiquitin Thiolesterase* or "Ubiquitin C-terminal hydrolase*" or "Ubiquitin C-Terminal Esterase*" or "Ubiquitin Carboxy-Terminal Hydrolase*" or "Ubiquitin Carboxy-Terminal Esterase*" or uch-l1 or UCHL1).ti,ab.
39.	(S100* or GFAP or "glial fibrillary acid* protein*" or "brain-derived neurotrophic factor*" or "brain-derived nerve growth factor*" or BDNF or spectrin* or tau or proteomic* or microRNA* or miRNA* or micro-rna*).ti,ab.
40.	((muscle or nervous or neuron* or alpha or beta or gamma) adj3 enolase*).ti,ab.
41.	(Phosphopyruvate Hydratase* or 2-phosphoglycerate* or 2-phospho-D-glycerate* or NSE).ti,ab.
42.	((neurofilament* adj3 (protein* or chain* or polypeptide*)) or NF-L or NF-H).ti,ab.
43.	((myelin basic or nerve tissue* or golli* or hog* or mbp*) adj2 protein*).ti,ab.
44.	((extracellular or secretory) adj vesicle*) or exovesicle* or apoptotic bod* or exosome* or endosome* or ectosome* or microvesicle* or ((membrane or cell-derived) adj microparticle*).ti,ab.
45.	biomarker*.ti,ab,kf.
46.	marker*.ti,ab.
47.	or/26-46
48.	25 and 47
49.	randomized controlled trial.pt.
50.	controlled clinical trial.pt.
51.	randomi#ed.ti,ab.
52.	placebo.ab.
53.	randomly.ti,ab.
54.	Clinical Trials as topic.sh.
55.	trial.ti.
56.	or/49-55
57.	Meta-Analysis/
58.	exp Meta-Analysis as Topic/
59.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
60.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
61.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
62.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
63.	(search* adj4 literature).ab.
64.	(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.
65.	cochrane.jw.
66.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
67.	or/57-66
68.	Epidemiologic studies/

69.	Observational study/
70.	exp Cohort studies/
71.	(cohort adj (study or studies or analys* or data)).ti,ab.
72.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
73.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
74.	Controlled Before-After Studies/
75.	Historically Controlled Study/
76.	Interrupted Time Series Analysis/
77.	(before adj2 after adj2 (study or studies or data)).ti,ab.
78.	exp case control study/
79.	case control*.ti,ab.
80.	Cross-sectional studies/
81.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
82.	or/68-81
83.	exp "Sensitivity and Specificity"/
84.	(sensitivity or specificity).ti,ab.
85.	((pre test or pretest or post test) adj probability).ti,ab.
86.	(predictive value* or PPV or NPV).ti,ab.
87.	likelihood ratio*.ti,ab.
88.	Likelihood Functions/
89.	((area under adj4 curve) or AUC).ti,ab.
90.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
91.	gold standard.ab.
92.	exp Diagnostic Errors/
93.	(false positiv* or false negativ*).ti,ab.
94.	Diagnosis, Differential/
95.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness or precision or validat* or validity or differential or error*)).ti,ab.
96.	or/83-95
97.	48 and (56 or 67 or 82 or 96)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial) 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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	*biological marker/
28.	*protein S 100/
29.	*glial fibrillary acidic protein/
30.	*enolase/
31.	*ubiquitin thiolesterase/
32.	exp *microRNA/
33.	*brain derived neurotrophic factor/
34.	*neurofilament protein/
35.	*spectrin/
36.	*myelin basic protein/
37.	*exosome/
38.	*tau protein/
39.	(Ubiquitin Thiolesterase* or "Ubiquitin C-terminal hydrolase*" or "Ubiquitin C-Terminal Esterase*" or "Ubiquitin Carboxy-Terminal Hydrolase*" or "Ubiquitin Carboxy-Terminal Esterase*" or uch-l1 or UCHL1).ti,ab.
40.	(S100* or GFAP or "glial fibrillary acid* protein*" or "brain-derived neurotrophic factor*" or "brain-derived nerve growth factor*" or BDNF or spectrin* or tau or proteomic* or microRNA* or miRNA* or micro-rna*).ti,ab.
41.	((muscle or nervous or neuron* or alpha or beta or gamma) adj3 enolase*).ti,ab.
42.	(Phosphopyruvate Hydratase* or 2-phosphoglycerate* or 2-phospho-D-glycerate* or NSE).ti,ab.
43.	((neurofilament* adj3 (protein* or chain* or polypeptide*)) or NF-L or NF-H).ti,ab.
44.	((myelin basic or nerve tissue* or golli* or hog* or mbp*) adj2 protein*).ti,ab.

45.	((extracellular or secretory) adj vesicle*) or exovesicle* or apoptotic bod* or exosome* or endosome* or ectosome* or microvesicle* or ((membrane or cell-derived) adj microparticle*)).ti,ab.
46.	biomarker*.ti,ab,kw.
47.	marker*.ti,ab.
48.	or/27-47
49.	26 and 48
50.	random*.ti,ab.
51.	factorial*.ti,ab.
52.	(crossover* or cross over*).ti,ab.
53.	((doubl* or singl*) adj blind*).ti,ab.
54.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
55.	crossover procedure/
56.	single blind procedure/
57.	randomized controlled trial/
58.	double blind procedure/
59.	or/50-58
60.	systematic review/
61.	Meta-Analysis/
62.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
63.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
64.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
65.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
66.	(search* adj4 literature).ab.
67.	(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.
68.	cochrane.jw.
69.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
70.	or/60-69
71.	Clinical study/
72.	Observational study/
73.	Family study/
74.	Longitudinal study/
75.	Retrospective study/
76.	Prospective study/
77.	Cohort analysis/
78.	Follow-up/
79.	cohort*.ti,ab.
80.	78 and 79
81.	(cohort adj (study or studies or analys* or data)).ti,ab.
82.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.

83.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
84.	(before adj2 after adj2 (study or studies or data)).ti,ab.
85.	exp case control study/
86.	case control*.ti,ab.
87.	cross-sectional study/
88.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
89.	or/71-77,80-89
90.	exp "sensitivity and specificity"/
91.	(sensitivity or specificity).ti,ab.
92.	((pre test or pretest or post test) adj probability).ti,ab.
93.	(predictive value* or PPV or NPV).ti,ab.
94.	likelihood ratio*.ti,ab.
95.	((area under adj4 curve) or AUC).ti,ab.
96.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
97.	diagnostic accuracy/
98.	diagnostic test accuracy study/
99.	gold standard.ab.
100.	exp diagnostic error/
101.	(false positiv* or false negativ*).ti,ab.
102.	differential diagnosis/
103.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness or precision or validat* or validity or differential or error*)).ti,ab.
104.	or/90-103
105.	49 and (59 or 70 or 89 or 104)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*))) :ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	MeSH descriptor: [Biomarkers] explode all trees
#13.	MeSH descriptor: [S100 Proteins] explode all trees
#14.	MeSH descriptor: [Glial Fibrillary Acidic Protein] this term only
#15.	MeSH descriptor: [Phosphopyruvate Hydratase] this term only

#16.	MeSH descriptor: [Ubiquitin Thiolesterase] this term only
#17.	MeSH descriptor: [MicroRNAs] explode all trees
#18.	MeSH descriptor: [Brain-Derived Neurotrophic Factor] this term only
#19.	MeSH descriptor: [Neurofilament Proteins] this term only
#20.	MeSH descriptor: [Spectrin] this term only
#21.	MeSH descriptor: [Myelin Basic Protein] this term only
#22.	MeSH descriptor: [Extracellular Vesicles] explode all trees
#23.	MeSH descriptor: [tau Proteins] this term only
#24.	(Ubiquitin Thiolesterase* or "Ubiquitin C-terminal hydrolase*" or "Ubiquitin C-Terminal Esterase*" or "Ubiquitin Carboxy-Terminal Hydrolase*" or "Ubiquitin Carboxy-Terminal Esterase*" or uch-l1 or UCHL1):ti,ab
#25.	(S100* or GFAP or "glial fibrillary acid* protein*" or "brain-derived neurotrophic factor*" or "brain-derived nerve growth factor*" or BDNF or spectrin* or tau or proteomic* or microRNA* or miRNA* or micro-rna*):ti,ab
#26.	((muscle or nervous or neuron* or alpha or beta or gamma) near/3 enolase*):ti,ab
#27.	(Phosphopyruvate Hydratase* or 2phosphoglycerate* or 2phospho-D-glycerate* or NSE):ti,ab
#28.	((neurofilament* near/3 (protein* or chain* or polypeptide*)) or NF-L or NF-H):ti,ab
#29.	((myelin basic or nerve tissue* or golli* or hog* or mbp*) near/2 protein*):ti,ab
#30.	((extracellular or secretory) near vesicle*) or exovesicle* or apoptotic bod* or exosome* or endosome* or ectosome* or microvesicle* or ((membrane or cell-derived) near microparticle*):ti,ab
#31.	biomarker*:ti,ab,kw
#32.	marker*:ti,ab
#33.	#12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32
#34.	#11 and #33

Epistemonikos search terms

1.	(advanced_title_en:(((trauma OR traumatic) AND (injury OR injuries))) OR advanced_abstract_en:(((trauma OR traumatic) AND (injury OR injuries)))) OR (advanced_title_en:(((skull OR cranial) AND fracture*)) OR advanced_abstract_en:(((skull OR cranial) AND fracture*))) OR (advanced_title_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*))) OR advanced_abstract_en:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))) AND (advanced_title_en:(biomarker* OR marker*) OR advanced_abstract_en:(biomarker* OR marker*)) OR (advanced_title_en:(S100* OR GFAP OR "glial fibrillary acid* protein*" OR "brain-derived neurotrophic factor*" OR "brain-derived nerve growth factor*" OR BDNF OR spectrin* OR tau OR proteomic* OR microRNA* OR miRNA* OR micro-rna*)) OR advanced_abstract_en:(S100* OR GFAP OR "glial fibrillary acid* protein*" OR "brain-derived neurotrophic factor*" OR "brain-derived nerve growth factor*" OR BDNF OR spectrin* OR tau OR proteomic* OR microRNA* OR miRNA* OR micro-rna*)) OR (advanced_title_en:(Ubiquitin Thiolesterase* OR "Ubiquitin C-terminal hydrolase*" OR "Ubiquitin C-Terminal Esterase*" OR "Ubiquitin Carboxy-Terminal Hydrolase*" OR "Ubiquitin Carboxy-Terminal Esterase*" OR uch-l1 OR UCHL1)) OR advanced_abstract_en:(Ubiquitin Thiolesterase* OR "Ubiquitin C-terminal hydrolase*" OR "Ubiquitin C-Terminal Esterase*" OR "Ubiquitin Carboxy-Terminal Hydrolase*" OR "Ubiquitin Carboxy-Terminal Esterase*" OR uch-l1 OR UCHL1)) OR (advanced_title_en:(enolase* OR Phosphopyruvate Hydratase* OR 2-phosphoglycerate* OR 2-phospho-D-glycerate* OR NSE)) OR advanced_abstract_en:(enolase* OR Phosphopyruvate
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	Hydratase* OR 2-phosphoglycerate* OR 2-phospho-D-glycerate* OR NSE))) OR (advanced_title_en:((neurofilament protein* OR myelin basic protein* OR extracellular vesicle* OR exovesicle* OR apoptotic bod* OR exosome* OR endosome* OR ectosome* OR microvesicle* OR cell-derived microparticle*)) OR advanced_abstract_en:((neurofilament protein* OR myelin basic protein* OR extracellular vesicle* OR exovesicle* OR apoptotic bod* OR exosome* OR endosome* OR ectosome* OR microvesicle* OR cell-derived microparticle*)))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

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

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title]) AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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
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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])

Head Injury Cervical Spine 2.4a/b

This literature search strategy was used for the following review:

- What is the diagnostic accuracy of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?
- What is the clinical and cost effectiveness of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.{NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	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	

Medline (Ovid) search terms

1.	exp Spinal Injuries/
2.	Spinal Cord Injuries/
3.	exp Neck Injuries/
4.	whiplash.ti,ab.
5.	((neck or spine or spinal) adj3 (trauma or injur* or fracture*)).ti,ab.
6.	or/1-5
7.	cervical.ti,ab.
8.	6 and 7

9.	(cervical adj3 (trauma* or injur* or fracture*)).ti,ab.
10.	8 or 9
11.	letter/
12.	editorial/
13.	news/
14.	exp historical article/
15.	Anecdotes as Topic/
16.	comment/
17.	case report/
18.	(letter or comment*).ti.
19.	or/11-18
20.	randomized controlled trial/ or random*.ti,ab.
21.	19 not 20
22.	animals/ not humans/
23.	exp Animals, Laboratory/
24.	exp Animal Experimentation/
25.	exp Models, Animal/
26.	exp Rodentia/
27.	(rat or rats or mouse or mice or rodent*).ti.
28.	or/21-27
29.	10 not 28
30.	limit 29 to English language
31.	tomography/
32.	exp magnetic resonance imaging/
33.	exp tomography, emission-computed/
34.	exp tomography, x-ray/
35.	Radiography/
36.	Neuroradiography/
37.	(compute* adj2 tomograph*).ti,ab.
38.	(CT or CAT or PET or SPECT).ti,ab.
39.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph*)).ti,ab.
40.	MRI.ti,ab.
41.	(radiograph* or xray* or x-ray* or x ray*).ti,ab.
42.	or/31-41
43.	30 and 42

Embase (Ovid) search terms

1.	spine injury/
2.	cervical spine injury/
3.	spinal cord injury/
4.	cervical spinal cord injury/
5.	neck injury/

6.	whiplash injury/
7.	whiplash.ti,ab.
8.	((neck or spine or spinal) adj3 (trauma or injur*)).ti,ab.
9.	or/1-8
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	(conference abstract or conference paper).pt.
14.	case report/ or case study/
15.	(letter or comment*).ti.
16.	or/10-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animal/ not human/
20.	nonhuman/
21.	exp Animal Experiment/
22.	exp Experimental Animal/
23.	animal model/
24.	exp Rodent/
25.	(rat or rats or mouse or mice or rodent*).ti.
26.	or/18-25
27.	9 not 26
28.	limit 27 to English language
29.	tomography/
30.	brain tomography/
31.	exp computer assisted tomography/
32.	exp emission tomography/
33.	exp nuclear magnetic resonance imaging/
34.	radiography/
35.	(compute* adj2 tomograph*).ti,ab.
36.	(CT or CAT or PET or SPECT).ti,ab.
37.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph*)).ti,ab.
38.	MRI.ti,ab.
39.	(radiograph* or xray* or x-ray* or x ray*).ti,ab.
40.	neuroradiology/ or brain radiography/
41.	or/29-40
42.	28 and 41

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Spinal Injuries] explode all trees
#2.	MeSH descriptor: [Spinal Cord Injuries] this term only
#3.	MeSH descriptor: [Neck Injuries] explode all trees

#4.	whiplash:ti,ab
#5.	((neck or spine or spinal) near/3 (trauma or injur* or fracture*)):ti,ab
#6.	#1 or #2 or #3 or #4 or #5
#7.	cervical:ti,ab
#8.	#6 and #7
#9.	(cervical near/3 (trauma* or injur* or fracture*)):ti,ab
#10.	#8 or #9
#11.	MeSH descriptor: [Tomography] this term only
#12.	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#13.	MeSH descriptor: [Tomography, Emission-Computed] explode all trees
#14.	MeSH descriptor: [Tomography, X-Ray] explode all trees
#15.	MeSH descriptor: [Radiography] this term only
#16.	MeSH descriptor: [Neuroradiography] this term only
#17.	(compute* near/2 tomograph*):ti,ab
#18.	(CT or CAT or PET or SPECT):ti,ab
#19.	((MR or magnetic resonance or NMR) near/2 (imag* or tomograph* or angiograph*)):ti,ab
#20.	MRI:ti,ab
#21.	(radiograph* or xray* or x-ray* or x ray*):ti,ab
#22.	#11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21
#23.	#10 and #22

A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies
	Quality of Life 1946 – 22 June 2022	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

Database	Dates searched	Search filters and limits applied
	Quality of Life 1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception – 31 st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31 st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

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/32-61
63.	25 and (42 or 62)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/

29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
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#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	((skull or cranial) adj3 fracture*)
#9.	((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Anticoagulants 3.1

This literature search strategy was used for the following review:

- How long should people who are on anticoagulant or antiplatelet therapy be observed in hospital after normal brain imaging or no indication for early imaging?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
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Embase (OVID)	1974 – 22 June 2022	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	Exclusions (conference abstracts)
Epistemonikos (The Epistemonikos Foundation)	Inception to 22 June 2022	Exclusions (Cochrane reviews)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) 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.	exp anticoagulants/ or coumarins/ or exp antithrombins/ or exp factor xa inhibitors/ or exp Thrombolytic Therapy/ or exp Fibrinolytic Agents/
27.	(anticoagul* anti-coagul* or antithrom* or anti-thromb* or DOAC or DOACs or thrombolytic*).ti,ab,kf.
28.	(blood adj thin*).ti,ab,kf.
29.	((thrombus or blood clot*) adj3 (prevent* or stop* or inhibit*)).ti,ab,kf.
30.	((thrombin or xa) adj2 inhibitor*).ti,ab,kf.
31.	warfarin.ti,ab,kf.
32.	(coumarin* or coumadin*).ti,ab,kf.
33.	(Edoxaban or Lixiana).ti,ab,kf.
34.	(Dabigatran or Pradaxa).ti,ab,kf.
35.	(Apixaban or Eliquis).ti,ab,kf.
36.	Heparin.ti,ab,kf.
37.	(Rivaroxaban or Xarelto or acetylsalicylic acid).ti,ab,kf.
38.	Phenindione.ti,ab,kf.
39.	(vitamin k adj2 (antagonist* or inhibit*)).ti,ab,kf.
40.	(antivitamin k or anti vitamin k).ti,ab,kf.
41.	(Acenocoumarol or Sinthrome).ti,ab,kf.
42.	exp platelet aggregation inhibitors/
43.	(antiplatelet* or anti-platelet* or antiaggregant* or anti-aggregant*).ti,ab,kf.
44.	(platelet* adj2 (inhibit* or antagonist* or aggregat*)).ti,ab,kf.
45.	aspirin.ti,ab,kf.

46.	(Cangrelor or Kengrexal).ti,ab,kf.
47.	Cilostazol.ti,ab,kf.
48.	Clopidogrel.ti,ab,kf.
49.	(Dipyridamole or Molita).ti,ab,kf.
50.	(Prasugrel or Efient).ti,ab,kf.
51.	(Selexipag or Upravi or prostacyclin).ti,ab,kf.
52.	(Ticagrelor or Brilique).ti,ab,kf.
53.	(Epoprostenol or Veletri or prostacyclin).ti,ab,kf.
54.	(Eptifibatide or Integrilin).ti,ab,kf.
55.	(Tirofiban or Aggrastat).ti,ab,kf.
56.	or/26-55
57.	25 and 56

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial) 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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	exp *anticoagulant agent/

28.	(anticoagul* anti-coagul* or antithromb* or anti-thromb* or DOAC or DOACs or thrombolytic*).ti,ab,kf.
29.	(blood adj thin*).ti,ab,kf.
30.	((thrombus or blood clot*) adj3 (prevent* or stop* or inhibit*)).ti,ab,kf.
31.	exp *antithrombin/ or exp *blood clotting factor 10a inhibitor/ or *blood clotting inhibitor/
32.	((thrombin or xa) adj2 inhibitor*).ti,ab,kf.
33.	warfarin.ti,ab,kf.
34.	*coumarin derivative/
35.	(coumarin* or coumadin*).ti,ab,kf.
36.	(Edoxaban or Lixiana).ti,ab,kf.
37.	(Dabigatran or Pradaxa).ti,ab,kf.
38.	(Apixaban or Eliquis).ti,ab,kf.
39.	Heparin.ti,ab,kf.
40.	(Rivaroxaban or Xarelto or acetylsalicylic acid).ti,ab,kf.
41.	Phenindione.ti,ab,kf.
42.	(vitamin k adj2 (antagonist* or inhibit*)).ti,ab,kf.
43.	(antivitamin k or anti vitamin k).ti,ab,kf.
44.	(Acenocoumarol or Sinthrome).ti,ab,kf.
45.	exp *antithrombocytic agent/
46.	(antiplatlet* or anti-platelet* or antiaggregant* or anti-aggregant*).ti,ab,kf.
47.	(platlet* adj2 (inhibit* or antagonist* or aggregat*)).ti,ab,kf.
48.	aspirin.ti,ab,kf.
49.	(Cangrelor or Kengrexal).ti,ab,kf.
50.	Cilostazol.ti,ab,kf.
51.	Clopidogrel.ti,ab,kf.
52.	(Dipyridamole or Molita).ti,ab,kf.
53.	(Prasugrel or Efiel).ti,ab,kf.
54.	(Selexipag or Upravi or prostacyclin).ti,ab,kf.
55.	(Ticagrelor or Brilique).ti,ab,kf.
56.	(Epoprostenol or Veletri).ti,ab,kf.
57.	(Eptifibatide or Integrilin).ti,ab,kf.
58.	(Tirofiban or Aggrastat).ti,ab,kf.
59.	or/27-58
60.	26 and 59

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees

#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*)):ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	conference:pt or (clinicaltrials or trialsearch):so
#13.	#11 NOT #12
#14.	MeSH descriptor: [Anticoagulants] explode all trees
#15.	MeSH descriptor: [Coumarins] explode all trees
#16.	MeSH descriptor: [Antithrombins] explode all trees
#17.	MeSH descriptor: [Factor Xa Inhibitors] explode all trees
#18.	MeSH descriptor: [Thrombolytic Therapy] explode all trees
#19.	MeSH descriptor: [Fibrinolytic Agents] explode all trees
#20.	(anticoagul* anti-coagul* or antithrom* or anti-thromb* or DOAC or DOACs or thrombolytic*):ti,ab
#21.	(blood near/1 thin*):ti,ab
#22.	((thrombus or blood clot*) near/3 (prevent* or stop* or inhibit*)):ti,ab
#23.	((thrombin or xa) near/2 inhibitor*):ti,ab
#24.	warfarin:ti,ab
#25.	(coumarin* or coumadin*):ti,ab
#26.	(Edoxaban or Lixiana):ti,ab
#27.	(Dabigatran or Pradaxa):ti,ab
#28.	(Apixaban or Eliquis):ti,ab
#29.	Heparin:ti,ab
#30.	(Rivaroxaban or Xarelto or acetylsalicylic acid):ti,ab
#31.	Phenindione:ti,ab
#32.	(vitamin k near/2 (antagonist* or inhibit*)):ti,ab
#33.	(antivitamin k or anti vitamin k):ti,ab
#34.	(Acenocoumarol or Sintrome):ti,ab
#35.	MeSH descriptor: [Platelet Aggregation Inhibitors] explode all trees
#36.	(antiplatelet* or anti-platelet* or antiaggregant* or anti-aggregant*):ti,ab
#37.	(platelet* near/2 (inhibit* or antagonist* or aggregat*)):ti,ab
#38.	aspirin:ti,ab
#39.	(Cangrelor or Kengrexal):ti,ab
#40.	Cilostazol:ti,ab
#41.	Clopidogrel:ti,ab
#42.	(Dipyridamole or Molita):ti,ab
#43.	(Prasugrel or Efient):ti,ab
#44.	(Selexipag or Upravi or prostacyclin):ti,ab
#45.	(Ticagrelor or Brilique):ti,ab
#46.	(Epoprostenol or Veletri or prostacyclin):ti,ab

#47.	(Eptifibatide or Integrilin):ti,ab
#48.	(Tirofiban or Aggrastat):ti,ab
#49.	(or #14-#48)
#50.	#13 and #49

Epistemonikos search terms

1.	(title:(((trauma OR traumatic) AND (injury OR injuries))) OR abstract:(((trauma OR traumatic) AND (injury OR injuries)))) OR (title:(((skull OR cranial) AND fracture*)) OR abstract:(((skull OR cranial) AND fracture*)) OR (title:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)) OR abstract:(((head OR brain OR craniocerebral OR cranial OR cerebral OR skull) AND (injur* OR trauma*)))))
2.	(title:(anticoagul* anti-coagul* OR antithrom* OR anti-thromb* OR DOAC OR DOACs OR thrombolytic*)) OR abstract:(anticoagul* anti-coagul* OR antithrom* OR anti-thromb* OR DOAC OR DOACs OR thrombolytic*)) OR (title:(blood AND thin*)) OR abstract:(blood AND thin*)) OR (title:(((thrombus OR blood clot*) AND (prevent* OR stop* OR inhibit*))) OR abstract:(((thrombus OR blood clot*) AND (prevent* OR stop* OR inhibit*))) OR (title:(((thrombin OR xa) AND inhibitor*)) OR abstract:(((thrombin OR xa) AND inhibitor*)) OR (title:(warfarin* OR coumarin* OR coumadin* OR Edoxaban OR Lixiana OR Dabigatran OR Rivaroxaban OR Xarelto OR acetylsalicylic acid OR Phenindione OR antivitamin k OR anti vitamin k OR Acenocoumarol OR Sintrome)) OR abstract:(warfarin* OR coumarin* OR coumadin* OR Edoxaban OR Lixiana OR Dabigatran OR Rivaroxaban OR Xarelto OR acetylsalicylic acid OR Phenindione OR antivitamin k OR anti vitamin k OR Acenocoumarol OR Sintrome)) OR (title:(vitamin k AND (antagonist* OR inhibit*))) OR abstract:(vitamin k AND (antagonist* OR inhibit*))) OR (title:(antiplatlet* OR anti-platelet* OR antiaggregant* OR anti-aggregant*)) OR abstract:(antiplatlet* OR anti-platelet* OR antiaggregant* OR anti-aggregant*)) OR (title:(platelet* AND (inhibit* OR antagonist* OR aggregat*)) OR abstract:(platelet* AND (inhibit* OR antagonist* OR aggregat*))) OR (title:(aspirin OR Cangrelor OR Kengrexal OR Cilostazol OR Clopidogrel OR Dipyridamole OR Molita OR Prasugrel OR Efiend OR Selexipag OR Upravi OR prostacyclin OR Ticagrelor OR Brilique OR Epoprostenol OR Veletri OR prostacyclin OR Eptifibatide OR Integrilin OR Tirofiban OR Aggrastat)) OR abstract:(aspirin OR Cangrelor OR Kengrexal OR Cilostazol OR Clopidogrel OR Dipyridamole OR Molita OR Prasugrel OR Efiend OR Selexipag OR Upravi OR prostacyclin OR Ticagrelor OR Brilique OR Epoprostenol OR Veletri OR prostacyclin OR Eptifibatide OR Integrilin OR Tirofiban OR Aggrastat))
3.	1 and 2

A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies

Database	Dates searched	Search filters and limits applied
	Quality of Life 1946 – 22 June 2022	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
	Quality of Life 1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31 st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31 st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Direct Access Imaging 3.2

This literature search strategy was used for the following review:

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

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 1: 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)

Medline (Ovid) search terms

<Click this field on the first page and insert footer text if required>

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.
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)

Embase (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.pt. or letter/
7.	note.pt.
8.	editorial.pt.
9.	(conference abstract or conference paper).pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/6-11
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 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)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Brain Concussion] explode all trees
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#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

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))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

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

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Intracranial Admission 3.3

This literature search strategy was used for the following review:

- What are the indications for hospital admission in people with all intracranial injuries?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	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	
Epistemonikos (The Epistemonikos Foundation)	Inception to 22 June 2022	Exclusions (Cochrane reviews)

Medline (Ovid) search terms

1.	craniocerebral trauma/ or exp brain injuries/ or exp head injuries, closed/ or exp intracranial hemorrhage, traumatic/ or exp skull fractures/
2.	((skull or cranial) adj3 fracture*).ti,ab,kf.

3.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab,kf.
4.	((trauma* or injur*) and (subdural or intracranial or epidural or subarachnoid)) adj2 (h?ematoma* or h?emorrhage* or bleed*).ti,ab,kf.
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.	Clinical Deterioration/
27.	*Hospitalization/
28.	*Patient Admission/
29.	*Patient discharge/
30.	(deteriorat* or hospitali?* or admission* or admit* or discharg* or monitor* or observ*).ti,ab,kf.
31.	or/26-30
32.	(Brain Injury Guideline* or Marshall or HSC DR or HSCDR).ti,ab,kf.
33.	abbreviated injury scale.ti,ab,kf.
34.	(risk adj2 (tool* or tree or rule* or assess* or factor* or scale*)).ti,ab,kf.
35.	((single or small) adj2 (bleed* or h?emorrhage*)).ti,ab,kf.
36.	(GCS or Glasgow coma scale).ti,ab,kf.
37.	((CT or CAT or compute* tomograph*) adj4 (positive* or finding* or confirm* or identif* or injur* or sever* or scale* or result* or outcome* or reading*)).ti,ab,kf.
38.	(blood* adj test*).ti,ab,kf.
39.	(pupillary adj2 (respons* or deficit* or abnormal or defect* or constrict* or reflex*)).ti,ab,kf.
40.	or/32-39

41.	25 and 31 and 40
42.	predict.ti.
43.	(validat* or rule*).ti,ab.
44.	(predict* and (outcome* or risk* or model*)).ti,ab.
45.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
46.	decision*.ti,ab. and Logistic models/
47.	(decision* and (model* or clinical*)).ti,ab.
48.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
49.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
50.	ROC curve/
51.	or/42-50
52.	Epidemiologic studies/
53.	Observational study/
54.	exp Cohort studies/
55.	(cohort adj (study or studies or analys* or data)).ti,ab.
56.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
57.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
58.	Controlled Before-After Studies/
59.	Historically Controlled Study/
60.	Interrupted Time Series Analysis/
61.	(before adj2 after adj2 (study or studies or data)).ti,ab.
62.	Cross-sectional studies/
63.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
64.	or/52-63
65.	Meta-Analysis/
66.	exp Meta-Analysis as Topic/
67.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
68.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
69.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
70.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
71.	(search* adj4 literature).ab.
72.	(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.
73.	cochrane.jw.
74.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
75.	or/65-74
76.	41 and (51 or 64 or 75)

Embase (Ovid) search terms

1.	*head injury/ or *brain injury/ or exp *brain hemorrhage/ or *skull injury/ or exp *skull fracture/
2.	((skull or cranial) adj3 fracture*).ti,ab,kf.
3.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab,kf.
4.	((((trauma* or injur*) and (subdural or intracranial or epidural or subarachnoid)) adj2 (h?ematoma* or h?emorrhage* or bleed*)).ti,ab,kf.
5.	or/1-4
6.	letter.pt. or letter/
7.	note.pt.
8.	editorial.pt.
9.	(conference abstract or conference paper).pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/6-11
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 or rodent*).ti.
22.	or/14-21
23.	5 not 22
24.	limit 23 to English language
25.	*Deterioration/
26.	*Hospitalization/
27.	*Hospital Admission/
28.	*Hospital Discharge/
29.	(deteriorat* or hospitali?* or admission* or admit* or discharg* or monitor* or observ*).ti,ab,kf.
30.	or/25-29
31.	(Brain Injury Guideline* or Marshall or HSC DR or HSCDR).ti,ab,kf.
32.	abbreviated injury scale.ti,ab,kf.
33.	(risk adj2 (tool* or tree or rule* or assess* or factor* or scale*)).ti,ab,kf.
34.	((single or small) adj2 (bleed* or h?emorrhage*)).ti,ab,kf.
35.	(GCS or Glasgow coma scale).ti,ab,kf.
36.	((CT or CAT or compute* tomograph*) adj4 (positive* or finding* or confirm* or identif* or injur* or sever* or scale* or result* or outcome* or reading*)).ti,ab,kf.
37.	(blood* adj test*).ti,ab,kf.

38.	(pupillary adj2 (respons* or deficit* or abnormal or defect* or constrict* or reflex*)).ti,ab,kf.
39.	or/31-38
40.	24 and 30 and 39
41.	predict.ti.
42.	(validat* or rule*).ti,ab.
43.	(predict* and (outcome* or risk* or model*)).ti,ab.
44.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
45.	decision*.ti,ab. and Statistical model/
46.	(decision* and (model* or clinical*)).ti,ab.
47.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
48.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
49.	Receiver operating characteristic/
50.	or/41-49
51.	Clinical study/
52.	Observational study/
53.	Family study/
54.	Longitudinal study/
55.	Retrospective study/
56.	Prospective study/
57.	Cohort analysis/
58.	Follow-up/
59.	cohort*.ti,ab.
60.	58 and 59
61.	(cohort adj (study or studies or analys* or data)).ti,ab.
62.	((follow up or observational or uncontrolled or non random#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
63.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
64.	(before adj2 after adj2 (study or studies or data)).ti,ab.
65.	cross-sectional study/
66.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
67.	or/51-57,60-66
68.	Meta-Analysis/
69.	exp Meta-Analysis as Topic/
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.	40 and (50 or 67 or 78)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#4.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#5.	MeSH descriptor: [Skull Fractures] explode all trees
#6.	(head or brain or craniocerebral or cranial or cerebral or skull) near/4 (injur* or trauma*):ti,ab
#7.	(trauma* or injur*) AND ((subdural or intracranial or epidural or subarachnoid) near/2 (h?ematoma* or h?emorrhage* or bleed*)):ti,ab
#8.	(or #1-#7)

Epistemonikos search terms

1.	(title:(title:(trauma* OR injur*)) OR abstract:(trauma* OR injur*)) AND (title:(subdural OR intracranial OR epidural OR subarachnoid)) OR abstract:(subdural OR intracranial OR epidural OR subarachnoid)) AND (title:(haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*) OR abstract:(haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*)) OR abstract:(title:(trauma* OR injur*)) OR abstract:(trauma* OR injur*)) AND (title:(subdural OR intracranial OR epidural OR subarachnoid)) OR abstract:(subdural OR intracranial OR epidural OR subarachnoid)) AND (title:(haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*) OR abstract:(haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies

Database	Dates searched	Search filters and limits applied
	Quality of Life 1946 – 22 June 2022	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
	Quality of Life 1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception – 31 st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31 st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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Head Injury Hypopituitarism 3.4/5

This literature search strategy was used for the following review:

- Which patients should be investigated for hypopituitarism after head injury?
- When should people with head injury be investigated for hypopituitarism?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.1 Clinical search literature search strategy

Searches were constructed using a Head Injury population and terms for Hypopituitarism. No filters were applied to cover both the intervention and diagnostic elements of the review.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	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)

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) 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.	Hypopituitarism/
27.	(Hypopituitarism* or hypopituitaryism* or PTHP).ti,ab.
28.	(pituitary adj2 (insufficien* or dysfunction* or injur* or damage* or function* or fail* or deficien* or hypofunction*)).ti,ab.
29.	(hypophysis adj2 (insufficien* or dysfunction* or injur* or damage* or function* or fail* or deficien* or hypofunction*)).ti,ab.
30.	Simmond* disease.ti,ab.
31.	or/26-30
32.	25 and 31

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 cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial) 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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	hypopituitarism/
28.	(Hypopituitarism* or hypopituitaryism* or PTHP).ti,ab.
29.	(pituitary adj2 (insufficien* or dysfunction* or injur* or damage* or function* or fail* or deficien* or hypofunction*)).ti,ab.
30.	(hypophysis adj2 (insufficien* or dysfunction* or injur* or damage* or function* or fail* or deficien* or hypofunction*)).ti,ab.
31.	Simmond* disease.ti,ab.
32.	or/27-30
33.	26 and 32

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Craniocerebral Trauma] this term only
#2.	MeSH descriptor: [Brain Injuries] explode all trees
#3.	MeSH descriptor: [Coma, Post-Head Injury] this term only
#4.	MeSH descriptor: [Head Injuries, Closed] explode all trees
#5.	MeSH descriptor: [Head Injuries, Penetrating] this term only
#6.	MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees
#7.	MeSH descriptor: [Skull Fractures] explode all trees
#8.	((skull or cranial) near/3 fracture*):ti,ab
#9.	((head or brain or craniocerebral or intracranial or cranial or skull) near/3 (injur* or trauma*)):ti,ab
#10.	(trauma* and ((subdural or intracranial) near/2 (h?ematoma* or h?emorrhage* or bleed*)):ti,ab
#11.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12.	MeSH descriptor: [Hypopituitarism] this term only
#13.	(Hypopituitarism* or hypopituitaryism* or PTHP):ti,ab
#14.	(pituitary near/2 (insufficien* or dysfunction* or injur* or damage* or function* or fail*)):ti,ab
#15.	Simmond* disease:ti,ab
#16.	#12 or #13 or #14 or #15

#17.	#11 and #16
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Epistemonikos search terms

1.	(title:(Hypopituitarism* OR hypopituitaryism* OR PTHP)) OR abstract:(Hypopituitarism* OR hypopituitaryism* OR PTHP)) OR (title:(pituitary AND (insufficien* OR dysfunction* OR injur* OR damage* OR function* OR fail* OR deficien* OR hypofunction*))) OR abstract:(pituitary AND (insufficien* OR dysfunction* OR injur* OR damage* OR function* OR fail* OR deficien* OR hypofunction*))) OR (title:(hypophysis AND (insufficien* OR dysfunction* OR injur* OR damage* OR function* OR fail* OR deficien* OR hypofunction*))) OR abstract:(hypophysis AND (insufficien* OR dysfunction* OR injur* OR damage* OR function* OR fail* OR deficien* OR hypofunction*))) OR (title:(Simmond* disease) OR abstract:(Simmond* disease))
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A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

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

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

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.

40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	<p>(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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])</p>
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Head Injury Skull Fractures 3.6

This literature search strategy was used for the following review:

- What is the rate of clinical deterioration in people with isolated skull fracture?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. {NICE2014}

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

A.1 Clinical search literature search strategy

Searches were constructed using a simplified Head Injury population focusing on Skull Fractures. Search filters were applied to the search where appropriate.

Table 1: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language

Medline (Ovid) search terms

1.	exp skull fractures/
2.	((skull or cranial) adj3 fracture*).ti,ab,kf.
3.	or/1-2
4.	letter/
5.	editorial/
6.	news/
7.	exp historical article/
8.	Anecdotes as Topic/
9.	comment/
10.	case report/

11.	(letter or comment*).ti.
12.	or/4-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animals/ not humans/
16.	exp Animals, Laboratory/
17.	exp Animal Experimentation/
18.	exp Models, Animal/
19.	exp Rodentia/
20.	(rat or rats or mouse or mice or rodent*).ti.
21.	or/14-20
22.	3 not 21
23.	limit 22 to English language
24.	Epidemiologic studies/
25.	Observational study/
26.	exp Cohort studies/
27.	(cohort adj (study or studies or analys* or data)).ti,ab.
28.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
29.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
30.	Controlled Before-After Studies/
31.	Historically Controlled Study/
32.	Interrupted Time Series Analysis/
33.	(before adj2 after adj2 (study or studies or data)).ti,ab.
34.	exp case control studies/
35.	case control*.ti,ab.
36.	Cross-sectional studies/
37.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
38.	or/24-37
39.	Meta-Analysis/
40.	exp Meta-Analysis as Topic/
41.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
42.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
43.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
44.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
45.	(search* adj4 literature).ab.
46.	(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.
47.	cochrane.jw.
48.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

49.	Or/39-48
50.	23 and (38 or 49)

Embase (Ovid) search terms

1.	exp skull fractures/
2.	((skull or cranial) adj3 fracture*).ti,ab,kf.
3.	or/1-2
4.	letter.pt. or letter/
5.	note.pt.
6.	editorial.pt.
7.	case report/ or case study/
8.	(letter or comment*).ti.
9.	(conference abstract or conference paper).pt.
10.	or/4-9
11.	randomized controlled trial/ or random*.ti,ab.
12.	10 not 11
13.	animal/ not human/
14.	nonhuman/
15.	exp Animal Experiment/
16.	exp Experimental Animal/
17.	animal model/
18.	exp Rodent/
19.	(rat or rats or mouse or mice or rodent*).ti.
20.	or/12-19
21.	3 not 20
22.	limit 21 to English language
23.	Clinical study/
24.	Observational study/
25.	family study/
26.	longitudinal study/
27.	retrospective study/
28.	prospective study/
29.	cohort analysis/
30.	follow-up/
31.	cohort*.ti,ab.
32.	30 and 31
33.	(cohort adj (study or studies or analys* or data)).ti,ab.
34.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
35.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
36.	(before adj2 after adj2 (study or studies or data)).ti,ab.

37.	exp case control study/
38.	case control*.ti,ab.
39.	cross-sectional study/
40.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
41.	or/23-29,32-40
42.	systematic review/
43.	meta-analysis/
44.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
45.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
46.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
47.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
48.	(search* adj4 literature).ab.
49.	(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.
50.	cochrane.jw.
51.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
52.	Or/42-51
53.	22 and (41 or 52)

A.2 Health Economics literature search strategy

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

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies
	Quality of Life 1946 – 22 June 2022	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

Database	Dates searched	Search filters and limits applied
	Quality of Life 1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception – 31 st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31 st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

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)

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.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/

29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/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)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
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#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	((skull or cranial) adj3 fracture*)
#9.	((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* 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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