National Institute for Health and Care Excellence

NICE guideline Head injury

[L] Evidence reviews for isolated skull fracture

NICE guideline NG232

Evidence reviews underpinning recommendation 1.9.1 to 1.9.5 in the NICE guideline

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Final

Developed by National Institute for Health and Care Excellence

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Isolated skull fracture

1.1 Review question

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

1.1.1 Introduction

Head trauma may result in injury to the skull and brain. These may occur together, or in isolation. Whilst some types of skull fracture (e.g., depressed skull fractures) are closely linked with underlying brain injury, simple linear skull fractures are often identified on CT scanning with no associated acute brain injury. Due to concerns that brain injury requiring neurosurgical intervention may subsequently develop, patients with isolated simple skull fractures are often admitted to hospital for observation. However, admission to hospital carries inherent risk of morbidity for the individual. If high quality evidence suggests subsequent deterioration is unlikely, it may be possible to safely discharge patients with isolated simple skull fracture after assessment in the Emergency Department, with benefits for patients, and the healthcare system.

1.1.2 Summary of the protocol

.Table 1: PICO characteristics of review question

Population	Inclusion: Infants, children and adults: • with isolated skull fractures and no intra cranial injury/abnormalities on imaging. Strata (i): • Adults (aged ≥16 years) • Children (aged ≥1 to <16 years) and • Infants (aged <1 year) Exclusion: • basal skull fracture • open fracture • depressed skull fracture • other intracranial injuries on CT scan Mixed population studies [(studies including both patients with isolated skull fracture and patients with intracranial injuries (intracranial bleeding, air, brain swelling or bruising) on CT scan] will be included– only if reported results separately for isolated skull fracture population. All people should have head CT – not just skull x-ray
Confounding factors	Key confounders (only isolated skull fracture population): • anti-coagulant/anti-platelet therapy or INR Key confounders for mixed population studies (If studies include both patients with isolated skull fracture and patients with intracranial injuries (intracranial bleeding, air, brain swelling or bruising) on CT scan): • anti-coagulant/anti-platelet therapy or INR • GCS (Glasgow Coma Scale)

Outcomes	All outcomes are considered equally important for decision making and therefore have all been rated as critical: -Clinical deterioration which includes: • Death within 30 days of injury • Neurosurgery within 30 days of injury • Need for critical care admission (within 30 days) • Reduction in GCS score (drop of 2 or more) (within 30 days) • Unplanned hospital re-admission at 30 days • delayed intracranial injury identified on repeated neuroimaging (within 30 days) • seizure, meningitis within 30 days of injury -Diagnosis of suspected abusive head trauma/non-accidental injury (NAI) within 3 months of injury
Study design	Prospective and retrospective cohort studies Case series Note: results from case series will only be reported at the group level (not at individual level). Case series for inclusion should have the format of introduction methods, results, and discussion/conclusions.

1.1.3 Methods and process

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

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

1.1.4 Prognostic evidence

1.1.4.1 Included studies

A search was conducted for cohort studies (prospective or retrospective), case series and systematic reviews including these study types to determine rate of clinical deterioration in people with isolated skull fracture and no intra cranial injury/abnormalities on imaging.

Twelve [10 retrospective and 2 prospective] case series were included in the review. [1, 4, 14, 15, 17, 20, 22, 28-30, 33, 37] these are summarised in below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

Population

All studies except one study were in infants and children. Some studies included only infants and some both infants and children. Age cut-off for children varied with some studies considering <16 years, <17 years, <18 or < 19 years as children. One study (Yavuz 2003) included both adults and children. There was no evidence for adults only population.

All studies except one were with isolated skull fracture. One study (Yavuz 2003) was in a mixed population (skull fracture+ intra cranial lesion). Mixed population studies were only included if the study reported results separately for people with isolated skull fracture.

Majority of the studies had people with GCS score =15 and two studies (Kommaraju 2019 and Hentzen 2015) had people with GCS score 14-15. Some studies did not report baseline GCS score.

Only one was multicentre (Metzger 2014) and rest were single centre studies.

Only studies using CT scan were included. Studies using skull x-ray or skull x-ray or CT or ultrasound were not included.

All studies were conducted in USA except for two studies (Reuveni-Salzman, 2016in Israel and Yavuz 2003 in Turkey). There were no studies conducted in the UK.

Outcomes

There was evidence for all outcomes except for outcome reduction of GCS.

Sample size

No sample size cut-offs specified in the protocol (n=100) were used for inclusion as there would be very few studies above this sample size cut-off and the committee wanted to review all relevant evidence for this population. Sample size of studies ranged from n=44 to n=3915.

Analysis

R code (metafor) was used for meta-analysis of single arm studies in isolated skull fracture population. For one study with mixed population (linear skull fracture vs linear skull fracture+ intra cranial lesion), pairwise meta-analyses were performed using Cochrane Review Manager (RevMan5).

See also the study selection flow chart in Appendix A, study evidence tables in Appendix D, forest plots in Appendix E and GRADE tables in Appendix F.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix J.

1.1.5 Summary of studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Population	Outcomes	Comments
Arrey, 2015 [1] Retrospective single arm (cases series) USA	N= 326 Children with isolated linear nondisplaced skull fractures (NDSFs) Linear skull fractures that crossed a suture line but did not have associated intracranial haemorrhage or other exclusion criteria were included Overall, the most common locations for an NDSF in this study were the occipital bone (n = 126), the parietal bone (n = 102), and the frontal bone (n = 58). Four percent of the patients had a nondisplaced frontal bone that extended to the orbital rim (n = 14) and 5% (n = 17) had a single fracture involving 2 bones. There were no frontal bone fractures that involved the frontal sinuses in this study. Age: Median 19 months Range 2 weeks–15 years Sex (M/F) 193/133 GCS: not reported	• Neurosurgery • Hospitalisation • Repeat admission • Seizures or seizure-like activity after head trauma • Non-accidental trauma evaluation	High risk of bias Analysis: single arm Not adjusted for key confounders No indirectness
Blackwood, 2016 [4] Retrospective single arm (cases series) USA	N= 71 Patients with isolated non-displaced skull fractures secondary to blunt head trauma with a normal neurological examination.	• Hospitalisation • Seizure • Neurosurgical intervention • Repeat head imaging • Re-admission	High risk of bias Analysis: single arm Not adjusted for key confounders

Study	Population	Outcomes	Comments
	Majority with unilateral parietal fracture. Age: Patient ages ranged from 1 week old to 12.4 years old with an average age of 19 months. Sixty of the total seventy-one patients (85%) were aged less than three years of age male: female: 56% were male and 44% were female. GCS score: 15		No indirectness
Hassan, 2014 [14] Retrospective single arm(cases series) USA	N= 233 with skull fracture (SF) [n=128 with non-depressed skull fracture with GCS score 15 considered for analysis] All had CT scan The SF group was divided into two groups, DSF (depressed skull fracture) and NDSF (non-depressed skull fracture). Each group was further subdivided into two groups based on their GCS score at presentation: GCS score of 15 and GCS score of less than 15. 128 children (78%) of the NDSF group presented with GCS score of 15 and n=35 with GCS<15. NDSF group, 128 children (78%) with GCS score of 15. Age: The mean (SD) age in this group was 21 (20) months, with a median of 12 months (range, 1 to73 months) Gender: NR	• Neurosurgical intervention • Mortality	High risk of bias Analysis: single arm Not adjusted for key confounders No indirectness Results reported for people with non-depressed skull fracture with GCS 15

Study	Population	Outcomes	Comments
	NDSF group had a GCS score of less than 15 on presentation. (N=35) The mean (SD) age in this group was 36 (21) months, with a median of 34 months (range, 8Y72 months) Gender: NR		
Hentzen, 2015 [15] Retrospective single arm study (cases series) USA	N= 65 Children (<17 years) with isolated skull fracture (ISF) identified without ICH on initial CT examination. Plain film radiography was not used to diagnose cranial injury Population characteristics: Age (years): 4.2 (4.6) Male sex: 35 (53.8%) The majority of patients had stable vital signs on admission. Most were also minimally injured as evidenced by a mean ISS of 7.2 (median = 5) and mean head/neck abbreviated injury score of 2.3 (median = 2). GCS: The average GCS score was 14.2 (median = 15) with 76.6% of the patients having a GCS score of 15. Children in this study showed a propensity for frontal and parietal fractures, with 17 children (26.2%) identified as having suffered a frontal fracture and 17 (26.2%) identified as having suffered a parietal fracture. These 2 fractures accounted for over 50% of all skull fractures identified. Other skull fractures	• Death • Neurosurgery • Unplanned hospital admission • Need for critical care admission • Delayed intra cranial injury • Seizure	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders Indirectness- included basilar and displaced fractures

Study	Population	Outcomes	Comments
	identified included occipital fractures (n =14, 21.5%), temporal fractures (n =10, 15.4%), basilar fractures (n =4, 6.2%), cribriform plate fracture (n =1, 1.5%), and mixed skull fractures (n =2, 3.1%). All but 2 of the patients in the study suffered displaced skull fractures (n= 63, 96.9%).		
Kommaraju, 2019 [17] Retrospective single arm (cases series) USA	N= 127 Children with isolated linear skull fracture (ILSF) Unilateral parietal fracture was the most common injury (n = 59, 46.5%) Age: 2.36 years (mean) Gender: Male 74 (58.3) Female 53 (41.7) GCS score: 14-15 On admission, GCS scores were 15 in 96.9% (n = 123) cases, and 14 in 3 cases. One patient with autism was nonverbal at baseline and had no reported score.	• Mortality • Neurosurgical intervention • Attending ED within 30 days after discharge • delayed intracranial injury identified on repeated neuroimaging • suspected nonaccidental trauma	High risk of bias Analysis: single arm Not adjusted for key confounders No indirectness
Mannix, 2013 [20] Retrospective single arm (cases series) USA	N= 3915 Children with isolated skull fracture (0-19 years) Age (IQR): 7 months (3 to 17 months) Gender: Male 2355 (60%) Female 1560 (40%) Admitted/discharged: 3069 (78%)/846 (22%)	• Death • Need for neurosurgery • ICU care • Re-admission within 72 hours • Skeletal survey imaging for /non-accidental injury ((NAI)	High risk of bias Analysis: single arm Not adjusted for key confounders No indirectness

Study	Population	Outcomes	Comments
	Isolated skull fracture was defined as nondisplaced skull fracture without evidence of intracranial haemorrhage, using ICD-9-CM codes (800.00 to 800.09), present on admission.		
Metzger, 2014 [22] Prospective single arm (cases series) USA	N=88 Children with isolated skull fracture (18 days to 16 years) Age, median (range): 10 months (18 days to 16 years) GCS score: 15 Skull fracture location: Parietal: 56 (64%) Occipital: 25 (28%) Upper temporal: 12 (14%) Frontal: 9 (10%) Multiple bones: 13 (15%) Isolated fracture: fracture with margins separated by <3mm; non-depressed or minimally depressed; no associated intracranial injury; not a basilar type fracture or to foramen magnum; no pneumacephalus.	• Death • Neurosurgery • Suspected non-accidental injury (NAI) • Unplanned admission to hospital • seizure	High risk of bias Analysis: single arm Not adjusted for key confounders No indirectness
Reid, 2012 [28] Retrospective single arm study (cases series) USA	N= 82 Children (< 2 years) with skull fracture. all had a head CT scan performed. All patients were found to have a linear, nondisplaced skull fracture. Of the reported fractures, 75 (82%) were parietal bone fractures, 7 (8%) were occipital, 6 (6%) were	• Death • Neurosurgery • Unplanned hospital admission • Delayed intra cranial injury • Seizure • Suspected non-accidental injury (NAI)	High risk of bias Not adjusted for key confounders Indirectness- included basilar fractures Study included n=92. Data extracted for children with isolated skull fracture (n=82). Children with intra cranial injury not included. Data was not reported separately for this group.

Study	Population	Outcomes	Comments
	frontal, 3 (3%) were basilar, and 1 (1%) involved both the parietal and occipital bones. Seventy-three patients (79%) were younger than 12 months, and 19 (21%) were between 12 and 24 months. 57 patients (62%) were male and 35 (38%) were female. GCS score: 15		
Reuveni-Salzman, 2016 [29] Retrospective single arm study (cases series) Israel	N= 222 Children (3 months-14 years) with isolated skull fracture (ISF) All had CT scan The most common fracture was in the parietal bone. Of single fractures, 67 (30.2 %) were in the parietal bone, 59 (26.6 %) in the frontal bone, 53 (23.9 %) in the occipital bone, and 11 (5 %) in the temporal bone. Fractures involved two or more bones were diagnosed in 32 (14.4 %) children Exclusion: children with known neurological deficit and children with skull base fractures. Age 3 months−1 year: 69 (31.1) 1–5 years: 98 (44.1) >5 years :55 (24.8)	• Neurosurgery • Unplanned hospital admission • Delayed intra cranial injury • Seizure • Suspected non-accidental injury (NAI)	High risk of bias Analysis: single arm Not adjusted for key confounders No indirectness

Study	Population	Outcomes	Comments
	N=152 (68.5 %) were male GCS score: 15		
Rollins, 2011 [30] Retrospective single arm study (cases series) USA	N= 235 Children (4-14 years) with isolated linear (and minimally displaced) closed fractures of the skull vault. All skull fractures were diagnosed using computed tomography (CT). Fracture location included parietal (110), occipital (72), frontal (28), temporal (10), and multiple bones (15). Median age: discharged n=58: 1.1 years Admitted n=177: 0.85 years GCS score: 15	• Death • Post-impact seizure • Unplanned hospital admission • Delayed intra cranial injury • Neurosurgery • Suspected non-accidental injury (NAI)	Analysis: single arm Not adjusted for key confounders No indirectness
Vogelbaum, 1998 [33] Prospective single arm study (cases series) USA	N= 44 Children (1 month-14.3 years) with uncomplicated skull fracture in minor heads injury Site of fracture included not reported. Patients were considered to have an `uncomplicated skull fracture' and were included in this review if they did not have intra- or extra-axial lesions on CT, did not require surgery for treatment of their head trauma, had a normal neurological examination and did not require surgery or hospitalisation for treatment of other injuries.	• Seizure • Suspected child abuse • Complication after injury • Neurosurgery	High risk of bias Analysis: single arm Not adjusted for key confounders No indirectness Skull x-ray and CT scan

Study	Population	Outcomes	Comments
	Age ranged in age from 1 month to 14.3 years (mean age 1.8 years). GCS score: 15		
Yavuz, 2003 [37] cases series Turkey	N= 500 Adults and children Depressed fracture: 69 Depressed fracture+intra cranial lesion: 49 Linear fracture: 152 Linear fracture+ intra cranial lesion= 92 Only intra cranial lesion: 138 Depressed fracture excluded in our protocol- so data is not extracted for this group. Data only included for linear fracture vs linear fracture+ intra cranial lesion Age Adults and children The mean age was 26.3 years. Of entire cases, 44.2% (n=221) were within age group 0–20 and 47.0% of cases (n=235) were within range of 21–50 years. 8.8% of cases were in 51 years and above. Most of cases having only linear fractures accumulated in the age group of 0–20. Gender	• Neurosurgical intervention	High risk of bias Analysis: mixed population (linear fracture vs linear fracture+ intra cranial lesion) Not adjusted for key confounders Both CT scan and skull x-ray used

Study	Population	Outcomes	Comments
	For males: 27.3% for only linear fractures and 18.3% for linear fractures plus intracranial lesion In female group: 39.8% for only linear fractures 18.7% for linear fractures and intracranial lesion GCS: not reported		

See Appendix D for full evidence tables

1.1.6 Summary of the evidence:

Clinical evidence summary: Isolated skull fracture– infants and children

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Effect estimate[d]	Proportion of people with events[e]
Death within 30 days of injury	n=4640 (7 case series) (Hassan 2014,Hentzen 2015, Kommaraju 2019, Mannix 2013, Metzger 2014 ,Reid 2012, Rollins 2011)	⊕◯◯◯ VERY LOW[a,b]	pred (ci.lb ci.ub) 0.0000 (0.0000 0.0000)	0 per 1000
Neurosurgery within 30 days of injury	n=2234 (11 case series) (Arrey 2015, Blackwood 2016, Hassan 2014, Hentzen	⊕◯◯◯ VERY LOW[a,b]	pred (ci.lb ci.ub) 0.0000 (0.0000 0.0005)	0 per 1000

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Effect estimate[d]	Proportion of people with events[e]
	2015,Kommaraju 2019,Mannix 2013,Metzger 2014,Reid 2012,Reuveni-Salzman 2016,Rollins 2011,Vogelbaum 1998)			
Need for critical care admission (within 30 days)	n=3980 (2 case series) (Hentzen 2015,Mannix 2013)	⊕◯◯◯ VERY LOW[a,B]	estimate 0.0467 0.0033	46 per 1000
Unplanned hospital re-admission at 30 days	n=2062 (9 case series) (Arrey 2015,Blackwood 2016,Hentzen 2015,Kommaraju 2019,Mannix 2013,Metzger 2014,Reid 2012,Reuveni-Salzman 2016,Rollins 2011)	⊕◯◯◯ VERY LOW[a,b,c]	pred (ci.lb ci.ub) 0.0057 (0.0002 0.0158)	57 per 10000
Delayed intracranial injury identified on repeated neuroimaging (within 30 days)	n=731 (5 case series) (Hentzen 2015, Kommaraju 2019,Reid 2012, Reuveni-Salzman 2016, Rollins 2011)	⊕◯◯◯ VERY LOW[a,b]	pred (ci.lb ci.ub) 0.0024 (0.0000 0.0088)	24 per 10000
Seizure within 30 days of injury	n=1133 (8 case series) (Arrey	⊕◯◯◯ VERY LOW[a,b]	pred (ci.lb ci.ub) 0.0082 (0.0029 0.0155)	82 per 10000

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Effect estimate[d]	Proportion of people with events[e]
[all were at presentation]	2015,Blackwood 2016, Hentzen 2015, Metzger 2014, Reid 2012, Reuveni-Salzman 2016, Rollins 2011, Vogelbaum 1998)			
Evaluations for suspected abusive head trauma/non-accidental injury (NAI) within 3 months of injury	n=5039 (8 case series) (Arrey 2015,Kommaraju 2019,Mannix 2013, Metzger 2014,Reid 2012,Reuveni-Salzman 2016, Rollins 2011, Vogelbaum 1998)	⊕◯◯◯ VERY LOW[a,b,c]	estimate (0.0916) SE (0.0479)	91 per 1000

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias and downgraded by 2 increments if the majority of the evidence was at very high risk of bias. Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series. Not adjusted for key confounders
b. Downgraded by 2 increment for indirectness. Two studies included basilar and displaced fractures. No studies conducted in the UK. All studies except one were conducted in the USA. One study was conducted in Israel.
c. Heterogeneity with fixed effects analysis. Random effects analysis used.
d. Estimate (SE) when there are no zero events in the data set. Pred values (CI) where there are zero events in the data set.
e. predicted proportion of people who had the outcome for that population

Table 3: Clinical evidence summary: Mixed population- linear fracture vs linear fracture + intra cranial lesion – Adults and children

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with linear fracture+intra cranial lesion	Risk difference with linear fracture
Neurosurgical intervention	244 (1 case series) (Yavuz, 2003)	⊕◯◯◯ VERY LOW[a,b]	OR 0.05 (0.02 to 0.13)	250 per 1,000	234 fewer per 1,000 (243 fewer to 208 fewer)[c]

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias and downgraded by 2 increments if the majority of the evidence was at very high risk of bias. Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series
b. Downgraded by 2 increment for indirectness. Includes both adults and children. Study conducted in Turkey. No study conducted in the UK.
c. Zero events in one arm. Peto odds ratio in Revman analysis and calculation of risk difference for absolute measure.

See Appendix F for full GRADE tables.

1.1.7 Economic evidence

1.1.7.1 Included studies

No health economic studies were included.

1.1.7.2 Excluded studies

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

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

1.1.8 Summary of included economic evidence

None.

1.1.9 Economic model

1.1.9.1 Model specification

Population: People with isolated skull fracture and no other indication for admission. All the clinical studies except one were in infants and children – see 1.1.4. In the base case analysis of the model, the age at time of injury was 2 years and ¾ of patients were male. In sensitivity analyses we looked at ages 18 years and 40 years.

Comparison: Admission for observation vs No admission

Outcomes: NHS cost, Quality-adjusted life-years (QALYs), Cost per QALY gained.

Details of this model can be found in Appendix I.

Model approach

The cost of the admission was attributed to all patients in the 'Admission' model arm. The proportion of patients that deteriorate requiring neurosurgery was taken from the guideline review. A treatment effect in terms of change in Glasgow Outcome Scale was applied only to the patients that deteriorate. Health state costs and utilities were applied to these patients. For all other patients, health state costs and utilities were not estimated, on the assumption that they would be the same in each arm.

Incidence of deterioration

The proportion of patients with isolated skull fracture that deteriorate after head injury was estimated from the guideline review – see 1.1.6:

- In the base case analysis, we used the estimate of based on the number of people reported to have deteriorated based on repeat CT scanning. This was 0.24% (0.00%, 0.88%)
- In a sensitivity analysis, we used the estimate of 0.045% (1/2234) based on the number needing neurosurgery in the review.

1.1.9.2 Model results

The base case was intentionally biased in favour of admission in the following ways:

- The estimate of the rate of deterioration most likely over-estimates the number of people requiring neurosurgery.
- The treatment effect was probably an over-estimate in terms of the number of cases of vegetative state averted.

- The age was low, and longer-term mortality was assumed to be no greater than the general population. Therefore, the life-years gained were maximised.

The cost per QALY gained for admission versus no admission was greater than £20,000 in the base case analysis (Table 4) and all the sensitivity analyses except where the effects were from Haselsberger 2010 (Table 5).

Table 4: Health economic evidence profile: Admissions for observation vs No admission for people with isolated skull fracture

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
NICE Methods and Economics Team 2022	Directly applicable	Minor limitations	• Markov model • Cost-utility analysis (QALYs) • Population: 2-year-old with isolated skull fracture Time horizon: lifetime	£312[(a)]	0.012 QALYs	£26,790 per QALY gained	The model was subject to various scenario analyses. The cost per QALY gained varied from £19,700 (using an alternative treatment effect size) to £221,000 (using the lower rate of deterioration).

Abbreviations: ICER= incremental cost-effectiveness ratio; QALY= quality-adjusted life years; RCT= randomised controlled trial
(a) 2021/22 UK pounds. Cost components incorporated: Hospital short stay plus long-term care costs (primary and secondary care) by Glasgow Outcome Scale category.

Table 5: Sensitivity analyses (deterministic)

Analysis	Isolated skull fracture population – Admission vs No admission		
	Incremental Cost	Incremental QALYs	Incremental cost per QALY gained
Base case results (probabilistic)	£308	0.0134	£22,922
Base case results (deterministic)	£312	0.0132	£23,711
Effect size (Glasgow Outcome Scale)			
Effects from Deverill 2007[9]	£531	0.0053	£99,970
Effects from Haselsberger 1988[13]	£453	0.0248	£18,293
Effects from Lecky 2016[18]	£493	0.0076	£64,658
Effects from Smits 2010[31]	£429	0.0155	£27,634
Deterioration probability			
Lower risk – 0.15%	£482	0.0025	£196,123
Age			
18 years	£390	0.0086	£45,224
40 years	£396	0.0073	£53,892
Other			
Standardised mortality ratio of 2.2 applied to mortality	£315	0.0128	£24,500
Utilities from Smits 2010[31]	£312	0.0142	£22,043

1.1.10 Unit costs

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

National Schedule of NHS Costs - Year 2019-20 version 2 - NHS trusts and NHS foundation trusts NON ELECTIVE SHORT STAY[24]			
Code	**Description**	**Number of Finished consultant episodes**	**National Average Unit Cost**
AA26C	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 15+	5,469	£1,256
AA26D	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 12-14	8,639	£654
AA26E	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 9-11	14,996	£580
AA26F	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 6-8	23,237	£520
AA26G	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 3-5	33,460	£465
AA26H	Muscular, Balance, Cranial or Peripheral Nerve Disorders, Epilepsy or Head Injury, with CC Score 0-2	31,230	£386
AA26	**Weighted average**	**117,031**	**£521**

1.1.11 Evidence statements

Economic

- One original cost–utility analysis found that admission for observation was not cost-effective (£22,900 per QALY gained) compared to no admission for people with isolated simple skull fracture on CT (even under favourable assumptions). This analysis was assessed as directly applicable with minor limitations.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The committee considered all outcomes as equally important for decision making and therefore have all been rated as critical: clinical deterioration which includes death within 30 days of injury, neurosurgery within 30 days of injury, need for critical care admission (within 30 days), reduction in GCS score (drop of 2 or more) (within 30 days), unplanned hospital re-admission at 30 days, delayed intracranial injury identified on repeated neuroimaging (within 30 days), seizure, meningitis within 30 days of injury and diagnosis of suspected abusive head trauma/non-accidental injury (NAI) within 3 months of injury.

There was evidence for all outcomes except for the outcome reduction of GCS score.

1.1.12.2 The quality of the evidence

Twelve [10 retrospective and 2 prospective] case series (single arm studies) were included in the review were included in the review. All studies except one study were in infants and children. One study included both adults and children. There was no evidence for adults only population. All studies except one were with isolated skull fracture. One study was in a mixed population (skull fracture+ intra cranial lesion).

The quality of outcomes was very low based on GRADE. Outcomes were commonly downgraded for risk of bias and indirectness. Outcomes were downgraded for risk of bias due to study design characteristics (retrospective, participants not recruited consecutively or cases from single centre). Some studies were deemed to have indirect evidence as they included people with basilar or depressed skull fractures which was not the population of interest in our review. The mixed population study (skull fracture+ intra cranial lesion) was downgraded for indirectness as it included both adults and children. The majority of the studies were conducted in the USA. These studies were assessed for applicability of evidence to the UK setting and were downgraded for indirectness. None of the studies adjusted for key confounders.

The assessment of clinically important results was based on the point estimate of predicted proportion of events for each outcome. For mortality any change was considered to be clinically important. For all other outcomes at least 100 cases or more per 1000 (10%) was considered to be clinically important.

The committee took into account the quality of the evidence in their interpretation of the evidence.

1.1.12.3 Benefits and harms

Isolated skull fracture- Infants and children

Evidence suggested that there was low risk of death, neurosurgery, critical care admission, unplanned hospital admission and delayed intra cranial injury in infants and children with isolated skull fracture.

There were no deaths in any of the studies. There was only one case needing neurosurgery, and the child was discharged after 2-day hospitalisation.

The committee discussed that for evidence based on studies in the USA, threshold for critical care admission is lower and the service and infra structure is different to the health care system in the UK. They noted that based on the baseline characteristics of the study participants (stable vital signs, mild GCS) none of them would be eligible for critical care admission under the current admission criteria in the UK. Most of the admissions to critical care are out of caution for observation.

None of the cases with unplanned hospital re-admission needed any medical intervention, they were all discharged after observation.

The committee noted that in the evidence for delayed intra cranial injury, in one of the cases, the second CT raised suspicion of minimal subarachnoid bleeding, which in retrospect was seen in the first CT as well. So, this was not delayed intra cranial bleeding or any deterioration, but the abnormality was missed at the initial CT. None of the cases with delayed intra cranial injury needed any medical intervention.

The evidence suggested that there was a slightly higher risk of seizure (at presentation) and evaluation for suspected non-accidental head injury (NAI) in this group. According to current guidelines (recommendations 1.4.7 and 1.4.9) people with seizure and suspected non-accidental injury (NAI) will be admitted to hospital after head injury.

Studies described fractures as simple, linear, non-depressed/non-displaced. Based on the evidence the committee agreed that these fractures are not likely to be clinically significant injury, hence infants and children with such fractures can be discharged safely if they have normal neurological status and no safeguarding concerns after shared decision making.

Mixed population (linear fracture vs linear fracture + intra cranial lesion)- adults and children

Evidence from one study suggested that there were fewer neurosurgical interventions in linear fracture group compared to linear fracture + intra cranial lesion group. This was found to be clinically important. There was no evidence for any other protocol outcome.

Isolated skull fracture- adults

There was no evidence for adults only with isolated skull fracture. For adults the committee considered indirect evidence from small intra cranial injuries review (see Evidence report K on small intra cranial injuries). Evidence suggested that there was low risk of clinical deterioration (composite of death due to traumatic brain injury (TBI), neurosurgery, seizure, >1 drop in GCS score, ICU admission for TBI, intubation or hospital readmission for TBI) in adults with simple skull fracture compared to those with complex skull fracture, 1-2 bleeds <5 mm in diameter, no or minimal mass effect, significant midline shift, high/mixed density lesion and cerebellar/brain stem injury. The simple skull fracture group included both isolated and non-isolated skull fracture, however the committee agreed that the evidence is still likely to be broadly applicable for adults with isolated skull fracture.

Based on indirect evidence and their collective experience the committee agreed that adults with isolated skull fracture can be discharged safely if there were no safety concerns after shared decision making.

Overall

Based on the evidence and their experience the committee agreed that people with isolated simple linear non-displaced skull fracture is unlikely to be a clinically significant abnormality hence recommended that these groups can be discharged safely if there are no safety concerns. These recommendations are applicable to adults, children and infants.

Due to lack of evidence specifically on people on anti-coagulants/anti-platelets, the committee wanted to be cautious and agreed that these groups of people can be admitted on clinical discretion.

Currently, most people with isolated skull fracture are admitted for observation. It is expected that many of these people could be discharged from the emergency department without admission to hospital unless there are other indications for admission.

1.1.12.4 Cost effectiveness and resource use

There were no published health economic evaluations of admission for people with isolated skull fracture. An original economic model was developed for children. Even under assumptions that were biased in favour of admission, with respect to incidence of adverse events, treatment effect and survival benefit, the cost per QALY gained was above £20,000 and under some plausible assumptions the cost per QALY exceeded £100,000. Only in one sensitivity analysis where there was a risk difference in mortality of 43% based on a cohort study from the 1980s did the cost per QALY gained dip below £20,000. For adults, the cost per QALY gained is likely to be higher than for children unless the risk of an adverse event is much higher.

The committee concluded that admission for people with isolated simple skull fracture and no other indication, is unlikely to be cost effective at £20,000 per QALY or at £30,000 per QALY for children or adults. They decided to recommend that isolated simple skull fracture should not be a reason for admission. This is expected to lead to a substantial resource saving, as currently most of these people are being admitted for observation.

1.1.12.5 Other factors the committee took into account

None.

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Appendices

Appendix A – Review protocols

Clinical review protocol for isolated skull fracture

ID	Field	Content
0.	PROSPERO registration number	CRD42022338148
1.	Review title	Isolated skull fracture Scope area: discharge and follow-up: 3.3 people with asymptomatic small intracranial injuries after imaging Q 3.3 included indications for admission of people with small intra cranial injuries. The population for this question was people with intra cranial injury on imaging (CT/MRI). Studies with skull fracture + intra cranial injury on imaging were included. Studies reporting isolated skull fracture without intra cranial injury were not included as they did not meet the protocol criteria. This review was presented in GC 8&9. Post-GC meeting the committee advised to consider inclusion of evidence with isolated skull fracture without intra cranial injury on imaging. Skull fracture is considered to be an intracranial injury because there will always be bleeding around the fracture site (otherwise the fracture can’t heal). Simple skull fractures affect intracranial integrity by weakening the skull (boundary of the intracranial space) - and hence simple skull fractures constitute an intracranial injury.

		Fractures may not be as benign as believed [there is evidence to show that blood biomarkers are raised in patients who only have skull fractures and no other abnormality detected on CT indicating that there is occult parenchymal injury (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8718895/]. Clinically significant abnormality on imaging is not defined. Clinical practice assumes at least some fractures may be significant and requires decisions about need for observation/rescanning etc so fractures should be considered in the recommendations/research recs.
2.	Review question	What is the rate of clinical deterioration in people with isolated skull fracture?
3.	Objective	To determine rate of clinical deterioration in people with isolated skull fracture and no intra cranial injury/abnormalities on imaging
4.	Searches	The following databases (from inception) will be searched: • Embase • MEDLINE Searches will be restricted by: • English language studies • Human studies Other searches: • Inclusion lists of systematic reviews The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.

		Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Isolated skull fracture
6.	Population	<u>Inclusion:</u> Infants, children and adults: • with isolated skull fractures and no intra cranial injury/abnormalities on imaging. Strata (i): • Adults (aged ≥16 years) • Children (aged ≥1 to <16 years) and • Infants (aged <1 year) <u>Exclusion</u> • basal skull fracture • open fracture • depressed skull fracture • other intracranial injuries on CT scan Note: CT scans do comment on scalp haematomas and wounds- these are not intra cranial injuries and population should not be excluded

		Mixed population studies [(studies including both patients with isolated skull fracture and patients with intracranial injuries (intracranial bleeding, air, brain swelling or bruising) on CT scan] will be included– only if reported results separately for isolated skull fracture population. All people should have head CT – not just skull x-ray People with isolated skull fractures and intra cranial injury on imaging will always have their risk of deterioration dominated by the intracranial injury. They will not be discharged Note: Prior to 2003- no head CT done only skull x-ray. If there was no fracture on skull x-ray, then head CT scan was done. If there was no fracture on skull x-ray it was just observation
9.	Types of study to be included	Prospective and retrospective cohort studies Case series Note: results from case series will only be reported at the group level (not at individual level). Case series for inclusion should have the format of introduction methods, results, and discussion/conclusions. Key confounders (only isolated skull fracture population): • anti-coagulant/anti-platelet therapy or INR Key confounders for mixed population studies (If studies include both patients with isolated skull fracture and patients with intracranial injuries (intracranial bleeding, air, brain swelling or bruising) on CT scan): • anti-coagulant/anti-platelet therapy or INR • Glasgow Coma Scale (GCS) <u>sample size- cut-off</u> n=100 in adults and children n=500 in mixed population studies
10.	Other exclusion criteria	Non-English language studies.

		Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available. Case reports
11.	Context	Skull fracture is considered to be an intracranial injury because there will always be bleeding around the fracture site (otherwise the fracture can't heal). Clinically significant abnormality on imaging is not defined. Clinical practice assumes at least some fractures may be significant and requires decisions about need for observation/rescanning etc so fractures should be considered in the recommendations/research recs.
12.	Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical: Clinical deterioration which includes: • Death within 30 days of injury • Neurosurgery within 30 days of injury • Need for critical care admission (within 30 days) • Reduction in GCS score (drop of 2 or more) (within 30 days) • Unplanned hospital re-admission at 30 days • delayed intracranial injury identified on repeated neuroimaging (within 30 days) • seizure, meningitis within 30 days of injury diagnosis of suspected abusive head trauma within 3 months of injury – based in history not imaging. Studies with only isolated skull fracture population (single arm studies): Number (%) of events In mixed population studies (comparing isolated skull fracture with other types of intra cranial injuries): In the absence of published MIDs, the default MIDs will be used as follows:

		For categorical outcomes: RRs of 0.8 and 1.25 For continuous outcomes: half the median standard deviation. For time to event data outcomes: HRs of 0.8 and 1.25
13.	Data extraction (selection and coding)	EndNote will be used for reference management, citations and bibliographies. All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
14.	Risk of bias (quality) assessment	For single arm studies (isolated skull fracture population only):

		Institute of Health Economics (IHE) checklist for case series http://www.ihe.ca/publications/ihe-quality-appraisal-checklist-for-case-series-studies For mixed population studies (Comparing isolated skull fracture with intra cranial injuries): Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.[Non-randomised study, including cohort studies: Cochrane ROBINS-I
15.	Strategy for data synthesis	For single arm studies: Meta analysis will be performed in R. Fixed and random effects models will be considered for the analysis with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models are deemed to be inappropriate if one or both of the following conditions was met: • Significant between study heterogeneity in methodology or population was identified by the reviewer in advance of data analysis. • The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$. If there is significant heterogeneity as defined above, results will be pooled using random effects. For mixed population studies: Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. Fixed-effects models are deemed to be inappropriate if one or both of the following conditions was met: • Significant between study heterogeneity in methodology or population was identified by the reviewer in advance of data analysis.

		• The presence of significant statistical heterogeneity in the meta-analysis, defined as I2≥50%. If there is significant heterogeneity as defined above, results will be pooled using random effects GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias will be considered with the guideline committee, and if suspected will be tested for when there are more than 5 studies for that outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ . • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. For more information please see the separate Methods report for this guideline.
16.	Analysis of sub-groups	None
17.	Type and method of review	☐ Intervention ☐ Diagnostic ☒ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
18.	Language	English

19.	Country	England		
20.	Anticipated or actual start date			
21.	Anticipated completion date			
22.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☐	☑
		Piloting of the study selection process	☐	☑
		Formal screening of search results against eligibility criteria	☐	☑
		Data extraction	☐	☑
		Risk of bias (quality) assessment	☐	☑
		Data analysis	☐	☑
23.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail headinjury@nice.org.uk		

		5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE)
24.	Review team members	From the National Guideline Centre: Guideline lead: Sharon Swain Senior systematic reviewer: Sharangini Rajesh Senior systematic reviewer: Julie Neilson Health economist: David Wonderling Information specialist: Joseph Runicles Project manager: Giulia Zuodar
25.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: 1 (nice.org.uk) .
28.	Other registration details	

29.	Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=338148	
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
31.	Keywords	Isolated skull fracture	
32.	Details of existing review of same topic by same authors		
33.	Current review status	☐	Ongoing
		☒	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
34.	Additional information		
35.	Details of final publication	www.nice.org.uk	

Table 6: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below. The search covered all years
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2006, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2006 or later that were included in the previous guidelines will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[23] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

	Where there is discretion The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2006 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2006 will be rated as ‘Not applicable’. • Studies published before 2006 (including any such studies included in the previous guidelines) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B – Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[23]

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

B.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 7: 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)

B.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 11: Database parameters, filters and limits applied

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

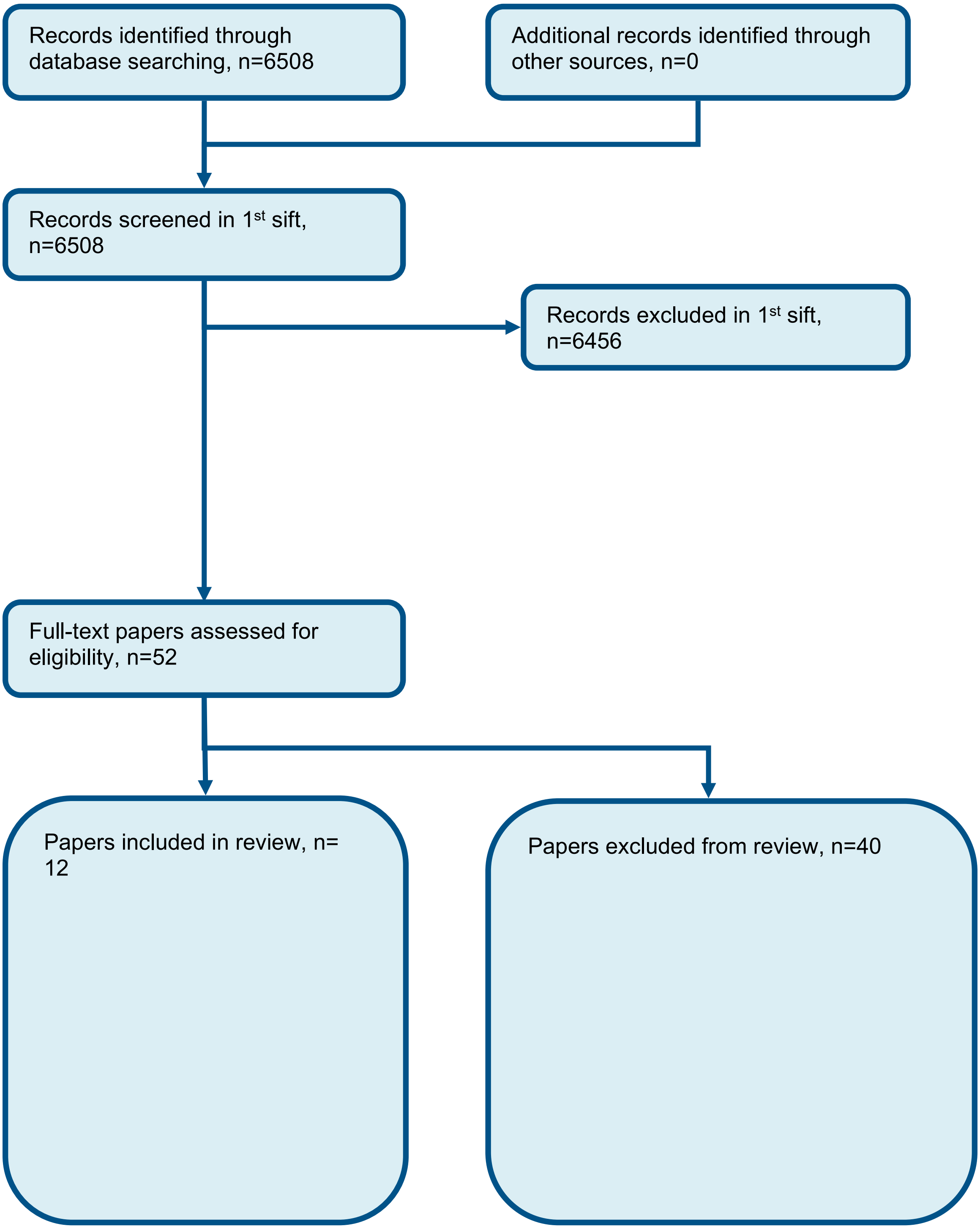
#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE 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])

Appendix C –Prognostic evidence study selection

Figure 1: Flow chart of clinical study selection for the review of isolated skull fracture



Appendix D – Prognostic evidence

Reference	Arrey, 2015 [1]
Study type Country	Retrospective single arm USA
Number of participants and characteristics	N= 326 study reviewed clinical management and outcomes in a large series of children with isolated linear nondisplaced skull fractures (NDSFs) **Inclusion criteria:** Patients with a single nondisplaced calvarial fracture were included in this study. Patients with isolated NDSFs and simultaneous non-CNS injuries (such as orthopaedic injuries) were included in the study. Linear skull fractures that crossed a suture line but did not have associated intracranial haemorrhage or other exclusion criteria were included **Exclusion criteria:** Patients with open or comminuted skull fractures, intracranial haemorrhage, multiple skull fractures, or pneumocephalus (defined as intracranial air) were excluded. Any quantity of intracranial haemorrhage or pneumocephalus, no matter how small, was sufficient for exclusion from this study. Patients with any other intracranial or cervical pathology such as hydrocephalus, brain tumors, head or neck vascular injuries, or cervical spine fractures were also excluded. **Population characteristics:** **Age:** Median 19 months Range 2 weeks–15 years **Sex (M/F)** 193/133 **Race/ethnicity** African American 27 Asian 16 Caucasian 126 Hispanic 148 Other* 9

Reference	Arrey, 2015 [1]
	GCS: not reported Overall, the most common locations for an NDSF in this study were the occipital bone (n = 126), the parietal bone (n = 102), and the frontal bone (n = 58). Four percent of the patients had a nondisplaced frontal bone that extended to the orbital rim (n = 14) and 5% (n = 17) had a single fracture involving 2 bones. There were no frontal bone fractures that involved the frontal sinuses in this study. **Population source:** retrospectively review of clinical records and imaging studies for patients between the ages of 0 and 16 years who were evaluated for NDSFs at Children's Memorial Hermann Hospital (CMHH) in Houston, Texas, between January 2009 and December 2013. All patients had received a CT scan at the time of diagnosis that clearly showed the NDSF in the bone window and any other intracranial pathology in the brain window
Comparator	NA
Confounders	Not reported
Outcomes	**Mortality:** not reported **Neurosurgery:** 0/326 **Hospitalisation:** 271/326 **Repeat admission:** 0/326 **Seizures or seizure-like activity after head trauma:** 8/326 **Non-accidental trauma evaluation:** 24/326 Of the 326 patients who met inclusion criteria, 56% (n = 184) were placed under 23-hour observation status, 27% (n = 87) were admitted to the hospital floor, and 17% (n =55) were discharged from the emergency department. Less than 16% (n = 50) were followed up in the paediatric neurosurgery clinic after discharge. All 50 of these patients were neurologically intact at the time of the follow-up visit. According to the history provided at the time of presentation to the emergency department, 14% of patients (n = 45) had altered mental status or loss of consciousness, 21% (n = 68) had at least 1 episode of vomiting after head trauma, and 2% (n = 8) had witnessed seizures or seizure-like activity after head trauma. No patient had any neurological deficits at the time of admission, and none required any neurosurgical intervention.

Reference	Arrey, 2015 [1]
	The mean hospital LOS for patients admitted to the inpatient unit was 46 hours, and the mean LOS for patients placed under 23-hour observation status was 18 hours. The LOS for patients in the inpatient unit ranged from 7 hours to 16days. The longest time a patient spent in the observation unit was 43 hours. Three percent of patients (n = 11) experienced extended hospitalization because of other injuries.
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders serious indirectness – study conducted in the USA

Reference	Blackwood, 2016 [4]
Study type Country	Retrospective single arm USA
Number of participants and characteristics	N= 71 Patients with isolated non-displaced skull fractures **Inclusion criteria:** patients presenting to the emergency department with CT of the head confirmed isolated non-displaced skull fractures secondary to blunt head trauma with a normal neurological examination. The neurologic exam was considered normal if no abnormality (no focal neurologic deficits, no witnessed seizures in the hospital setting, Glasgow Coma Scale (GCS) score = 15) was found in reviewing the documented physical examinations from the Trauma, Emergency Department (ED), and Neurosurgery physicians evaluating the patient at the time of presentation. All examinations included a full evaluation of gross motor function, sensory function, cranial nerve function, GCS, retrograde memory, and antegrade memory as appropriate to the age of the patient. **Exclusion criteria:** patients with penetrating head trauma, depressed skull fractures, skull fractures involving the skull base, presence of neurological deficits on physical examination, intracranial haemorrhage on imaging, pneumocephalus, or polytrauma.

Reference	Blackwood, 2016 [4]
	Population characteristics: **Age:** Patient ages ranged from 1 week old to 12.4 years old with an average age of 19 months. Sixty of the total seventy-one patients (85%) were aged less than three years of age **male : female:** 56% were male and 44% were female. **GCS** score: 15 Fracture type (N) percentage with 95% CI Discharged (n=16) admitted (n=55) - Unilateral parietal: 11 (68.8%; 41.3%,89.0%) 29 (52.7%; 38.8%,65.3%) p = 0.3910 - Bilateral parietal: 0 (0.00%) 3 (5.5%; 1.1%, 15.1%) p = 0.9999 - Unilateral occipital: 2 (12.5%; 1.6%,38.4%) 14 (25.5%; 14.7%,39.0%) p = 0.3335 - Bilateral occipital : 1 (6.3%; 0.2%, 30.2%) 0 (0.00%) p = 0.2254 - Unilateral frontal: 1 (6.3%; 0.2%, 30.3%) 6 (10.9%; 4.1%, 22.3%) p = 0.9999 - Bilateral frontal: 0 (0.0%) 1 (1.8%; 0.1%, 9.7%) p = 0.9999 - Combination: 1 (6.3%; 0.2%, 30.2%) 2 (3.6%; 0.4%, 12.5%) p = 0.5410 **Population source:** The medical records of all paediatric trauma patients presenting to the emergency department with ICD-9 codes indicating head trauma (803.00, 803.01, 803.06, 803.09, 854.00, 959.00, 660890, and 727915) were reviewed from June of 2004 through June of 2014.
Comparator	NA
Confounders	Not reported
Outcomes	**Hospitalisation:** 55/71 **Seizure:** 1/71 **Neurosurgical intervention:** 0/71 **Repeat head imaging:** 3/71 **Re-admission:** 0/71 **Mortality:** not reported **Non-accidental trauma**: not reported The majority (77.5%) of patients were admitted for inpatient neurological observation with serial neurological exams and 22.5% of patients were

Reference	Blackwood, 2016 [4]
	discharged from the emergency department with outpatient follow-up.
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders Serious indirectness- study conducted in the USA

Reference	Hassan, 2014 [14]
Study type Country	Retrospective single arm USA
Number of participants and characteristics	N= 233 with skull fracture (SF) [n=128 with non-depressed skull fracture with GCS score 15 considered for analysis] A total of 1,546 injured young children were evaluated during the study period. From this cohort, 563 children had isolated head injury, and 223 of them had only SF (the remaining 340 patients had no evidence of SF on initial computed tomography [CT] scans). The SF group was divided into two groups, DSF (depressed skull fracture) and NDSF (non-depressed skull fracture). Each group was further subdivided into two groups based on their GCS score at presentation: GCS score of 15 and GCS score of less than 15. 128 children (78%) of the NDSF group presented with GCS score of 15 and n=35 with GCS<15. **Inclusion criteria:** children with skull fracture **Exclusion criteria:** NR **Population characteristics:**

Reference	Hassan, 2014 [14]
	NDSF group, 128 children (78%) with GCS score of 15. The mean (SD) age in this group was 21 (20) months, with a median of 12 months (range, 1Y73 months) **Gender**: NR **NDSF group had a GCS score of less than 15 on presentation.** (N=35) The mean (SD) age in this group was 36 (21) months, with a median of 34 months (range, 8Y72 months) **Gender**: NR **Population source:** trauma registry at the University Hospital in San Antonio to identify all children 5 years or younger with an SF who presented to Level I trauma centre from January 2007 through December 2010.
Comparator	NA
Confounders	Not reported
Outcomes	**NDSF children with GCS** score **=15 (N=128)** **Neurosurgical intervention**: 0/128 **Mortality:** 0/128 **NDSF children with GCS** score **<15 (N=35)** **Mortality:** 2/35 (both of those patients had a GCS score of 3 on presentation). **Neurosurgical intervention**: 0/35
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders serious indirectness- study conducted in the USA

Reference	Hentzen, 2015 [15]
Study type Country	Retrospective single arm study USA
Number of participants and characteristics	N= 65 Children (<17 years) with isolated skull fracture (ISF) **Inclusion criteria:** Eligible patients were those with ISFs identified without ICH on initial CT examination. Plain film radiography was not used to diagnose cranial injury **Exclusion criteria:** subjects greater than 17 years of age, multisystem trauma, and identification of ICH on initial imaging of the brain **Population characteristics:** **Age (years):** 4.2 (4.6) **Male sex:** 35 (53.8%) The majority of patients had stable vital signs on admission. Most were also minimally injured as evidenced by a mean ISS of 7.2 (median 5 5) and mean head/neck abbreviated injury score of 2.3 (median 5 2). **GCS:** The average GCS score was 14.2 (median =15) with 76.6% of the patients having a GCS score of 15. Children in this study showed a propensity for frontal and parietal fractures, with 17 children (26.2%) identified as having suffered a frontal fracture and 17 (26.2%) identified as having suffered a parietal fracture. These 2 fractures accounted for over 50% of all skull fractures identified. Other skull fractures identified included occipital fractures (n =14, 21.5%), temporal fractures (n =10, 15.4%), basilar fractures (n= 4, 6.2%), cribriform plate fracture (n =1, 1.5%), and mixed skull fractures (n= 2, 3.1%). All but 2 of the patients in the study suffered displaced skull fractures (n =63, 96.9%). **Population source:** A retrospective study was conducted of all trauma patients 17 years of age or younger who sustained a skull fracture and were evaluated at an American College of Surgeons verified level I trauma centre between January 1, 2001, and December 31, 2011. Study subjects were identified by searching the trauma registry for International Classification of Diseases, Ninth Revision codes for skull fractures.
Comparator	NA

Reference	Hentzen, 2015 [15]
Confounders	NR
Outcomes	**Death:** 0/65 **Neurosurgery:** 0/65 **Unplanned hospital admission:** 0/65 **Need for critical care admission:** 41/65 **Delayed intra cranial injury:** 1/65 **Seizure:** 1/65 All the patients in the study were admitted to the hospital at least overnight, and the majority (63.1%) were monitored in the paediatric ICU, with an average ICU length of stay of 1.2 days (range 1 to 3 days). Only 4 children required mechanical ventilation because of their injury. Three of these presented to the hospital with a GCS score of 3 and were not breathing, and the fourth presented with a GCS score of 9 with respirations of 20 per minute. Three required less than 1 day of mechanical ventilation and 1 required 2 days of mechanical ventilation. The overall length of stay for this population was 1.7 days (median 5 1 day, range 1 to 7 days). Approximately two thirds of the children (67.7%) were hospitalised for 24 hours or less. The vast majority (96.9%) were able to be dismissed directly home and there were no deaths in this study population. One patient developed an ICH after her initial CT evaluation of the head. She had multiple indicators of head injury including a nonfrontal scalp hematoma, loss of consciousness, GCS score less than 15, and nausea. Her nausea continued for 72 hours and she developed a headache, which led to repeat CT of the head that revealed a small SDH (subdural haematoma). She was treated without neurosurgical intervention and was subsequently dismissed home.
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders Very serious indirectness- included basilar and displaced fractures. study conducted in the USA

Reference	Kommaraju, 2019 [17]
Study type	Retrospective chart review

Reference	Kommaraju, 2019 [17]
Country	A 10-year retrospective chart review at a Level 1 Paediatric Trauma Centre (2005-2015) USA
Number of participants and characteristics	N= 127 Children with isolated linear skull fracture (ILSF) American Academy of Paediatrics (AAP) definition of an ILSF to be a single fracture that is restricted to one bone with margins separated by <3 mm, is not depressed, and is devoid of other intracranial pathology **Inclusion criteria:** Children with isolated linear skull fracture (ILSF) **Exclusion criteria:** age >18 years, open or depressed fractures, skull base fractures, pneumocephalus, poly-trauma, intraparenchymal haemorrhage, epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, cervical spine fractures, penetrating head trauma, and initial GCS scores <13 **Population characteristics:** **Age:** 2.36 years (mean) **Gender:** Male 74 (58.3) Female 53 (41.7) **GCS** score: 14-15 On admission, GCS scores were 15 in 96.9% (n = 123) cases, and 14 in 3 cases. One patient with autism was nonverbal at baseline and had no reported score. The majority of patients were identified as Caucasian (n = 77, 60.6%) or African American (n = 36, 28.3%). Most of the injuries were due to falls (n = 103, 81.1%). Unilateral parietal fracture was the most common injury (n = 59, 46.5%). All patients underwent neurosurgical evaluation within the first 12 h of arrival to the institution.

Reference	Kommaraju, 2019 [17]
	On initial presentation to ED, 63.8% (n = 81) of patients were asymptomatic or back to baseline activity level per caregiver report. However, the most common symptoms documented were nausea and/or emesis (38.6%, n = 49), drowsiness (14.2%, n = 18), and headache (12.6%, n = 16), with the majority of symptomatology gone within 12–24 h of arrival Type of fracture: Parietal: 59 (46.5) Occipital: 29 (22.8) ≥2 vault bones: 13 (10.2) Parietal + temporal: 5 Biparietal: 4 Parietal + occipital: 4 Parietal + frontal: 2 Biparietal + temporal: 1 Temporal + occipital: 1 Bifrontal :1 Frontal + ipsilateral orbit: 9 (7.09) Frontal: 8 (6.30) Temporal: 5 (3.94) Diastatic: 2 (1.57) “Ping Pong”: 2 (1.57) **Population source:** Institutional Review Board approval was obtained to retrospectively analyse the Paediatric Trauma Registry Database at Virginia Commonwealth University Health System, an American College of Surgeons verified Level 1 Paediatric Trauma Centre.
Comparator	NA
Confounders	NR
Outcomes	**Mortality:** 0/127 **Neurosurgical intervention:** 0 /127 **Attending ED within 30 days after discharge**: 7/127 Seven patients returned to the ED within 30 days of hospital discharge. Two patients returned for a fever, and 1 patient returned for each of the following reasons: re-fall, upper respiratory tract infection, gastroenteritis, irritability, and unspecified.

Reference	Kommaraju, 2019 [17]
	Not clear if they were admitted. **delayed intracranial injury identified on repeated neuroimaging**: 0/127 Two patients underwent repeat head CT. One study was ordered by the primary paediatric surgery service to rule out a subdural haemorrhage that may have been missed on initial scan of poor quality. The second patient was less interactive on the following day. The primary paediatric service ordered this film. These patients were 1.45 and 1.13 years old, respectively. Repeat scans demonstrated no change from baseline **suspected non-accidental trauma:** n=7/127 patients documented as likely nonaccidental trauma
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders serious indirectness- study conducted in the USA

Reference	Mannix, 2013 [20]
Study type and analysis Country	Retrospective multi-centre cross-sectional study USA
Number of participants and characteristics	N= 3915 **Inclusion criteria:** children younger than 19 years, presenting to the ED at select children's hospitals in the USA between January 2005 and December 2011 who were assigned an ED diagnosis of skull fracture. Isolated skull fracture was defined as nondisplaced skull fracture without evidence of intracranial hemorrhage, using ICD-9-CM codes (800.00 to 800.09), present on admission. **Exclusion criteria:** patients with an admission diagnosis of intracranial bleeding (800.1 to 800.9, 801.x to 804.x), those with fractures of the base of the skull (802.xx), and children with a depressed skull fracture requiring elevation of skull fracture fragments (ICD-9-CM

Reference	Mannix, 2013 [20]
	procedure code 02.02); pervious diagnosis of skull fracture, intracranial hemorrhage, or neurosurgical procedure (01.x to 03.x) before ED arrival but during the study period; patients **Population characteristics: median age (IQR):** 7 months (3 to 17); gender m/f: 2355/1560 (60/40%); race: white 2668 (68%); black 667 (17%); other 185(5%); missing: 394 (10%):ED disposition: admitted 3069 (78%), discharged: 846 (22%). **Population source:** data were derived from the Pediatric Health Information System, administrative databased maintained by the Children's Hospital Association, with data from freestanding, tertiary care children's hospitals in 27 states and the District of Columbia.
Comparator	NA
Confounders	NR
Outcomes	Death :0/3915 Need for neurosurgery: 1/3915 (6 month year old had repair of the cerebral meninges) ICU care 176/3915 (4%) Re-admission (within 72 hours) 9/846 (1%) Skeletal survey imaging (for suspected non-accidental injury (NAI) : 186/3150 (6%).
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series: High risk of bias Not adjusted for key confounders serious indirectness- study conducted in the USA

Reference	Metzger, 2014 [22]
Study type and analysis Country	Prospective observational study USA
Number of participants and characteristics	N= 88 **Inclusion criteria:** skull fracture identified using CT; GCS score 15 on arrival. Isolated fracture: fracture with margins separated by <3mm; non-depressed or minimally depressed; no associated intracranial injury; not a basilar type fracture or to foramen magnum; no pneumacephalus. Skull fracture location: Parietal: 56 (64%) Occipital: 25 (28%) Upper temporal: 12 (14%) Frontal: 9 (10%) Multiple bones: 13 (15%) **Exclusion criteria:** other injuries that influenced admission status; a midface or basilar skull fracture (occipital fractures were included if not reaching the foramen magnum); a significantly displaced or depressed skull fracture; intracranial injury; the injury occurred more than one day prior to the initial evaluation. **Population characteristics:** • Age, median (range): 10 months (18 days to 16 years) • GCS score: 15 **Population source:** patients were from a paediatric level I trauma centre between February 2012 and February 2014. Enrolled at time of treatment or identified after discharge using information systems and ICD9 codes.
Comparator	NA
Confounders	NR
Outcomes	Non-accidental trauma: 10/88 Admission to hospital (during 2-year study period): 50/88 (57%)

Reference	Metzger, 2014 [22]
	Neurosurgery: 0/88 (0%) Death: 0/88 (0%) Seizure: 3/88
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series: High risk of bias Not adjusted for key confounders serious indirectness- study conducted in the USA

Reference	Reid, 2012 [28]
Study type Country	Retrospective single arm study USA
Number of participants and characteristics	N= 82 Children with skull fracture. All had a head CT scan performed. All patients were found to have a linear, non-displaced skull fracture. Of the reported fractures, 75 (82%) were parietal bone fractures, 7 (8%) were occipital, 6 (6%) were frontal, 3 (3%) were basilar, and 1 (1%) involved both the parietal and occipital bones. **Inclusion criteria:** Children with skull fracture. **Exclusion criteria:** if they suffered a depressed, diastatic, or open fracture; sustained a significant noncranial injury (eg, intrathoracic or intra-abdominal injury or long bone, spine, or facial fracture); or received their initial care at an outside institution **Population characteristics:** 57 patients (62%) were male and 35 (38%) were female. Seventy-three patients (79%) were younger than 12 months, and 19 (21%) were between 12 and 24 months.

Reference	Reid, 2012 [28]
	GCS score**:** 15 **Population source:** retrospective review of patients younger than 2 years who presented to the emergency department of an urban, university-affiliated, free-standing children's hospital from January 2003 through December 2010 and received a diagnosis of skull fracture
Comparator	NA
Confounders	Not reported
Outcomes	Primary outcome was significant intracranial injury was defined as death as a result of head injury, requirement of a neurosurgical intervention, tracheal intubation for a neurologic indication, or hospitalisation for more than 48 hours because of concerns related to head injury **Death:** 0/82 **Neurosurgery:** 0/82 **Unplanned hospital admission:** 0/82 **Delayed intra cranial injury:** 0/82 **Seizure:** 0/82 **Suspected non-accidental injury (NAI)**: 2/82
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders Very serious indirectness- included basilar and displaced fractures. study conducted in the USA Study included n=92. Data extracted for children with skull fracture only (n=82). Children with intra cranial injury not included. Data was not reported separately for this group.

Reference	Reuveni-Salzman, 2016 [29]
Study type Country	Retrospective single arm study Israel
Number of participants and characteristics	N= 222 Children with isolated skull fracture (ISF) Of the children aged 3 months to 14 years who arrived at the Hadassah Ein Kerem Hospital following head trauma from 2006 to 2012 and underwent a head CT between 1 to 24 h following a head injury, 222 met the study inclusion criteria. **Inclusion criteria:** e (1) aged 3 months to 14 years, (2) the occurrence of head trauma within 24 h prior to arrival at the emergency room, (3) Glasgow Coma Scale score of 15 at every stage from the first arrival to the emergency room, and (4) a proven linear or minimally compressed (up to 3 mm) ISF as demonstrated in non-contrast CT scan. With no neurological signs or symptoms, or other abnormal findings in imaging studies (i.e. intracranial hematoma, brain edema, etc.) **Exclusion criteria:** children with known neurological deficit and children with skull base fractures. **Population characteristics:** **Gender**: N=152 (68.5 %) were male **Age** 3 months−1 year: 69 (31.1) 1–5 years: 98 (44.1) >5 years :55 (24.8) **GCS** score**:** 15 The most common fracture was in the parietal bone. Of single fractures, 67 (30.2 %) were in the parietal bone, 59 (26.6 %) in the frontal bone, 53 (23.9 %) in the occipital bone, and 11 (5 %) in the temporal bone. Fractures involved two or more bones were diagnosed in 32 (14.4 %) children **Population source:** analysis data from the medical records of children who were hospitalized with ISF in the paediatric neurosurgery unit of the Hadassah Ein Kerem Hospital between January 2006 and December 2012 following head trauma

Reference	Reuveni-Salzman, 2016 [29]
Comparator	NA
Confounders	NR
Outcomes	**Neurosurgery:** 0/222 **Unplanned hospital admission:** 1/222 **Delayed intra cranial injury:** 1/222 **Seizure:** 0/222 **Suspected non-accidental injury (NAI):**: 2/222 Of the 222 children who were included in study, four (1.8 %) received a repeated CT exam. Two girls underwent a repeated CT during their initial hospitalisation, due to persistence/worsening of symptoms. In one of these cases the second CT raised suspicion of minimal subarachnoid bleeding, which in retrospect was seen in the first CT as well. No medical intervention was required, and both girls were discharged after observation. One month later, both girls were completely asymptomatic. Two other girls underwent a repeated imaging following an additional fall, one during her hospitalisation and one a few days later. For both girls the second CT did not demonstrate any new findings, and both were discharged after evaluation and clearance by the child abuse team. One boy suffered ongoing headaches for several days after discharge. A repeated CT scan revealed the same findings as the first one—a linear parietal fracture on the right side, without intracranial bleeding. He was hospitalised again for observation only and discharged without any need of intervention. According to the medical records, none of the children required neurosurgical intervention or were seen for re-consultation in the neurosurgical outpatient clinic following the injury (range of follow-up 2–8 years), indicating that none of the children had a growing skull fracture.
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders No indirectness

Reference	Rollins, 2011 [30]
Study type Country	Retrospective single arm study USA
Number of participants and characteristics	N= 235 **Inclusion criteria:** Children with isolated linear (and minimally displaced) closed fractures of the skull vault. All skull fractures were diagnosed using computed tomography (CT). **Exclusion criteria:** (1) other injuries that influenced their admission status; (2) a midface or basilar skull fracture (occipital fractures were included if not approaching the foramen magnum); (3) a large skull fracture where a width was stated in the record, or stated as “displaced” or “depressed” without use of the term “minimal”; (4) intracranial injury diagnosed at initial evaluation; and (5) the injury occurred more than 24 hours before hospital arrival. **Population characteristics:** **Age:** **Median age:** discharged n=58: 1.1 years Admitted n=177: 0.85 years **GCS** score**: 15** Fracture location included parietal (110), occipital (72), frontal (28), temporal (10), and multiple bones (15). **Population source:** A retrospective review of children seen at a tertiary level I trauma centre between January 1, 2003, and December 31, 2008, with a diagnosis of isolated linear (and minimally displaced) closed fractures of the skull vault was conducted. Patients with a diagnosis of closed skull fracture and a GCS score of 15 were identified using the hospital trauma registry and an ED database.
Comparator	NA
Confounders	Not reported
Outcomes	**Death:** 0/235 **Post-impact seizure:** 2/235 **Unplanned hospital admission:** 5/235

Reference	Rollins, 2011 [30]
	Delayed intra cranial injury: 1/235 **Neurosurgery:** 0/235 **Suspected non-accidental injury (NAI)**:: 2/235 Two patients had a postimpact seizure, 13 had a definite loss of consciousness, 15 had possible loss of consciousness, and 66 had vomiting before disposition from the ED (discharge or admission to observation unit or surgical ward). Only 26 patients had persistent symptoms, which included nausea and vomiting (18), amnesia (3), or headache (5) at the time of admission. Five patients who had been previously admitted for observation returned to the ED for recurrent symptoms within a few hours to 4 days following discharge. One of these patients developed vomiting on the day of discharge after overnight inpatient observation, and the repeat CT scan demonstrated a small extra-axial hematoma in the prepontine cistern. No intervention was needed, and he was discharged the following day after resolution of vomiting and photophobia. Repeat CT scans in the other four patients showed no new findings, and no specific interventions were rendered. No patient with an ISF who was discharged from the ED returned with symptoms.
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders Serious indirectness- study conducted in the USA

Reference	Vogelbaum, 1998 [33]
Study type Country	Prospective single arm study

Reference	Vogelbaum, 1998 [33]
	USA
Number of participants and characteristics	N= 44 Children with uncomplicated skull fracture in minor heads injury **Inclusion criteria:** uncomplicated skull fracture. Patients were considered to have an `uncomplicated skull fracture' and were included in this review if they did not have intra- or extra-axial lesions on CT, did not require surgery for treatment of their head trauma, had a normal neurological examination and did not require surgery or hospitalization for treatment of other injuries. **Exclusion criteria:** NR **Population characteristics**: **Age** They ranged in age from 1 month to 14.3 years (mean age 1.8 years). Nine patients (20%) presented with 1 or more episodes of emesis, and 3 patients (7%) had suffered brief LOC immediately after injury. No patient in this group had a seizure. Most patients (n = 35, 80%) had a scalp hematoma directly over the fracture, but only 3 patients (7%) had either a hemo-tympanum (1) or oto-/rhinorrhea (2). No patient had a Battle sign or focal neurological deficits. **GCS** score**:** 15 **Population source:** As part of a prospective paediatric head trauma study protocol in effect between January 1, 1993 and December 31, 1994, all minor head injury patients underwent skull radiographs, head CT scans, and had telephone follow-up conversations with their caregivers 24¬72 h after discharge from the emergency room or hospital. All children with skull fractures were routinely admitted to the hospital
Comparator	NA
Confounders	NA
Outcomes	**Seizure:** 0/44 **Suspected child abuse:** 22/44 **Complication after injury:** 0/44 **Neurosurgery:** 0/44
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series

Reference	Vogelbaum, 1998 [33]
	High risk of bias Not adjusted for key confounders serious indirectness- study conducted in the USA

Reference	Yavuz, 2003 [37]
Study type Country	Retrospective single arm study Turkey
Number of participants and characteristics	N= 500 Depressed fracture: 69 Depressed fracture+intra cranial lesion: 49 Linear fracture: 152 Linear fracture+ intra cranial lesion= 92 Only intra cranial lesion: 138 Depressed fracture excluded in our protocol- so data is not extracted for this group. People with skull fractures plus brain lesions, skull fractures with no brain lesions, brain lesions with no skull fractures – categorised based on cranium x-rays and brain tomographies.

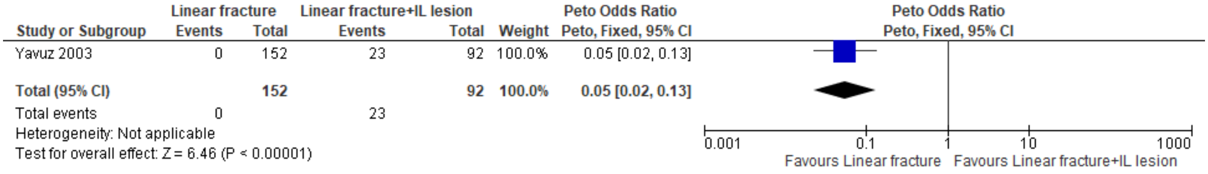
Reference	Yavuz, 2003 [37]
	Inclusion criteria: People with head injury in traffic accidents. Depending on their cranial x-ray and brain tomography findings, the cases having skull fractures and brain lesions, cases having skull fractures with no brain lesion and cases having brain lesion without any skull fractures were selected. **Exclusion criteria:** NR **Population characteristics:** Age Adults and children The mean age was 26.3 years. Of entire cases, 44.2% (n=221) were within age group 0–20 and 47.0% of cases (n=235) were within range of 21–50 years. 8.8% of cases were in 51 years and above. Most of cases having only linear fractures accumulated in the age group of 0–20. **Gender** For males: 27.3% for only linear fractures and , 18.3% for linear fractures plus intracranial lesion In female group: 39.8% for only linear fractures 18.7% for linear fractures and intracranial lesion Of the cases, 152 had only linear fractures. Among them, there were 45 (29.6%) in frontal, 28 (18.4%) occipital, 23 (15.1%) temporal and 22 (14.5%) cases in parietal bone. In the other cases (n=34), the fractures were related to more than one bone. Location of fractures among 92 cases having linear fractures and intracranial lesion are as follows: 22 (23.9%) frontal, 22 (23.9%) temporal, 18 (19.6) parietal and 11 (12.0%) occipital bones and in 19 cases (20.6%), fractures were related to more than one bone. **GCS:** not reported **Population source:** 500 cases, which were referred to the Third Committee of Council of Forensic Medicine in Istanbul due to traffic accidents by the courts of laws between 1998 and 2000, were examined retrospectively.
Comparator	Linear fracture only vs linear fracture+ intra cranial lesion
Confounders	NA
Outcomes	**Neurosurgical intervention:** Linear fracture only: 0/152

Reference	Yavuz, 2003 [37]
	Linear fracture+ intra cranial lesion: 23/92
Comments	Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series High risk of bias Not adjusted for key confounders Serious indirectness: mixed population (skull fracture+ intra cranial injury)

Appendix E – Forest plots

E.1 Linear fracture vs Linear fracture+ intra cranial lesion - adults and children

Figure 2: Neurosurgical intervention (lower is better)



E.2 Isolated skull fracture- infants and children

Figure 3: Mortality (lower is better)

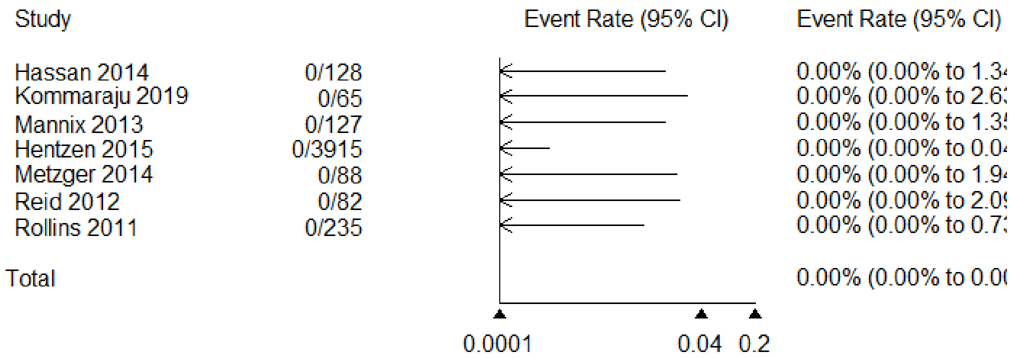


Figure 4: Need for neurosurgical intervention (lower is better)

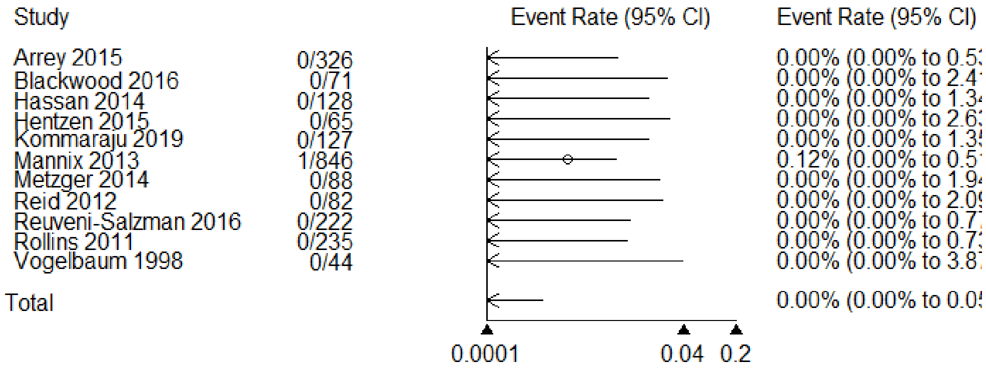


Figure 5: Need for critical care admission (lower is better)

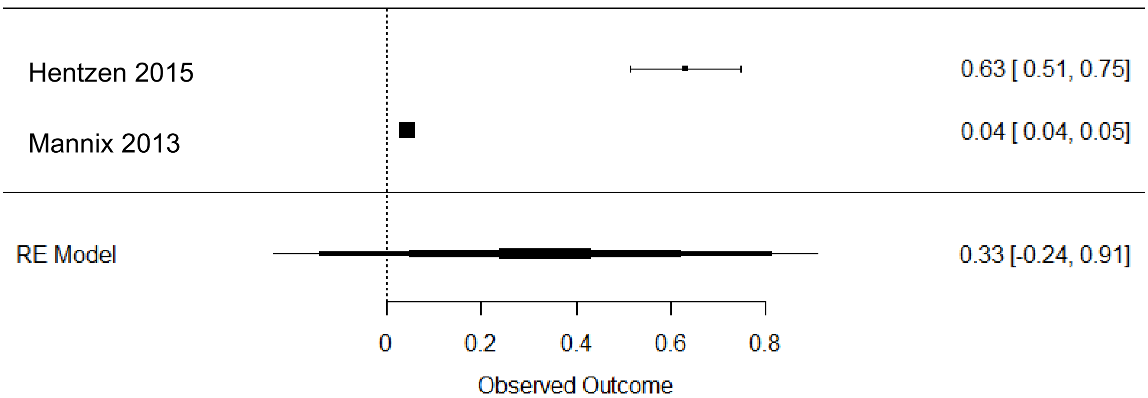


Figure 6: Unplanned hospital admission (lower is better)

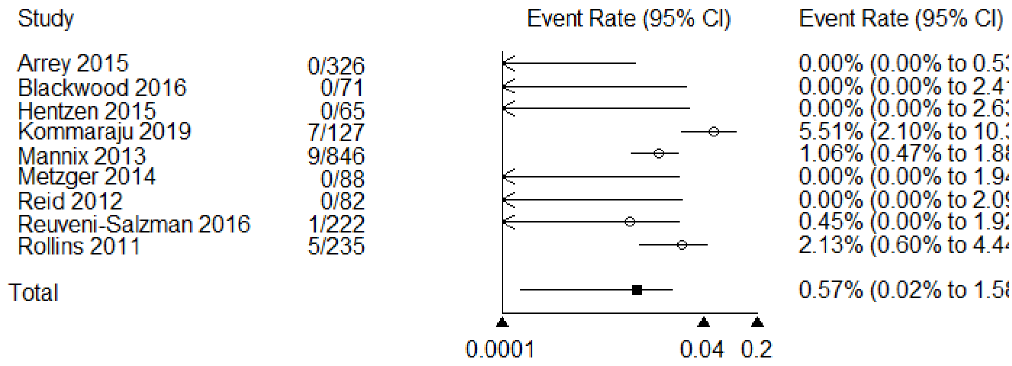


Figure 7: Delayed intra cranial injury (lower is better)

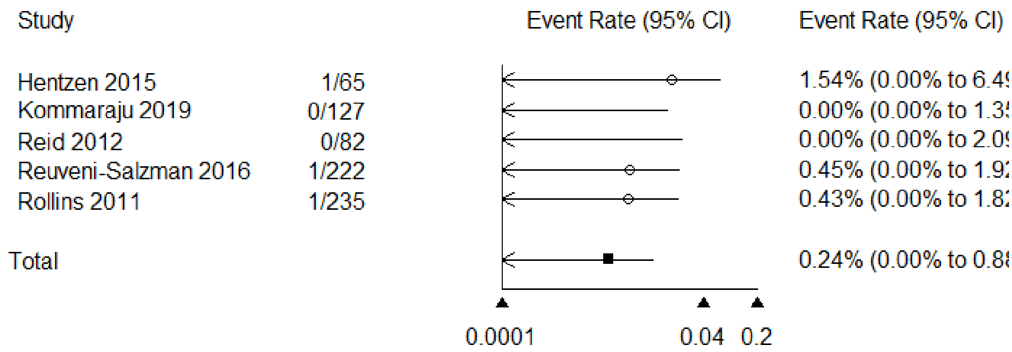


Figure 8: Seizure (lower is better)

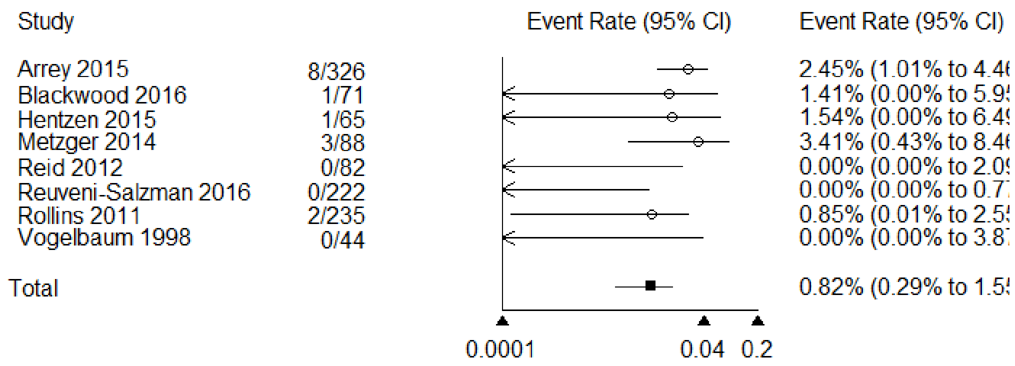
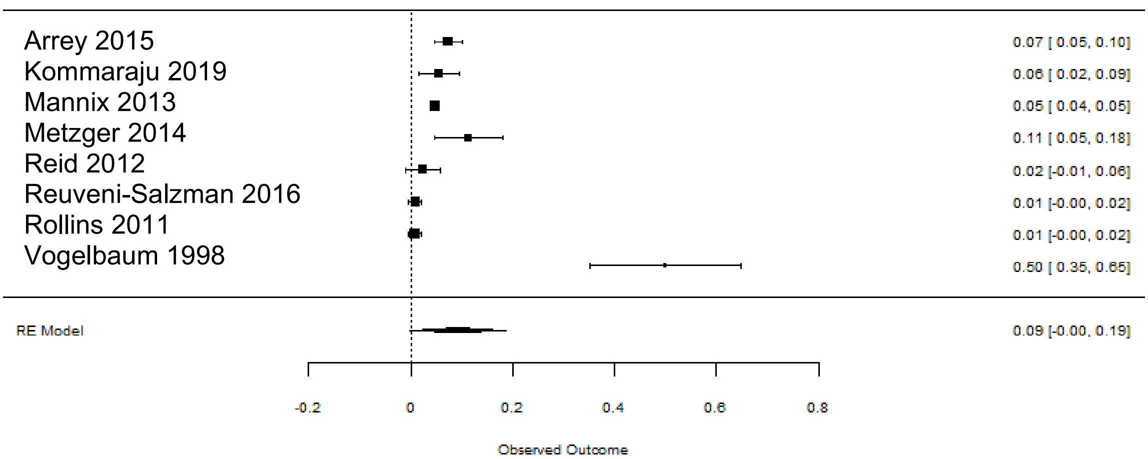


Figure 9: Suspected non-accidental injury (NAI) (lower is better)



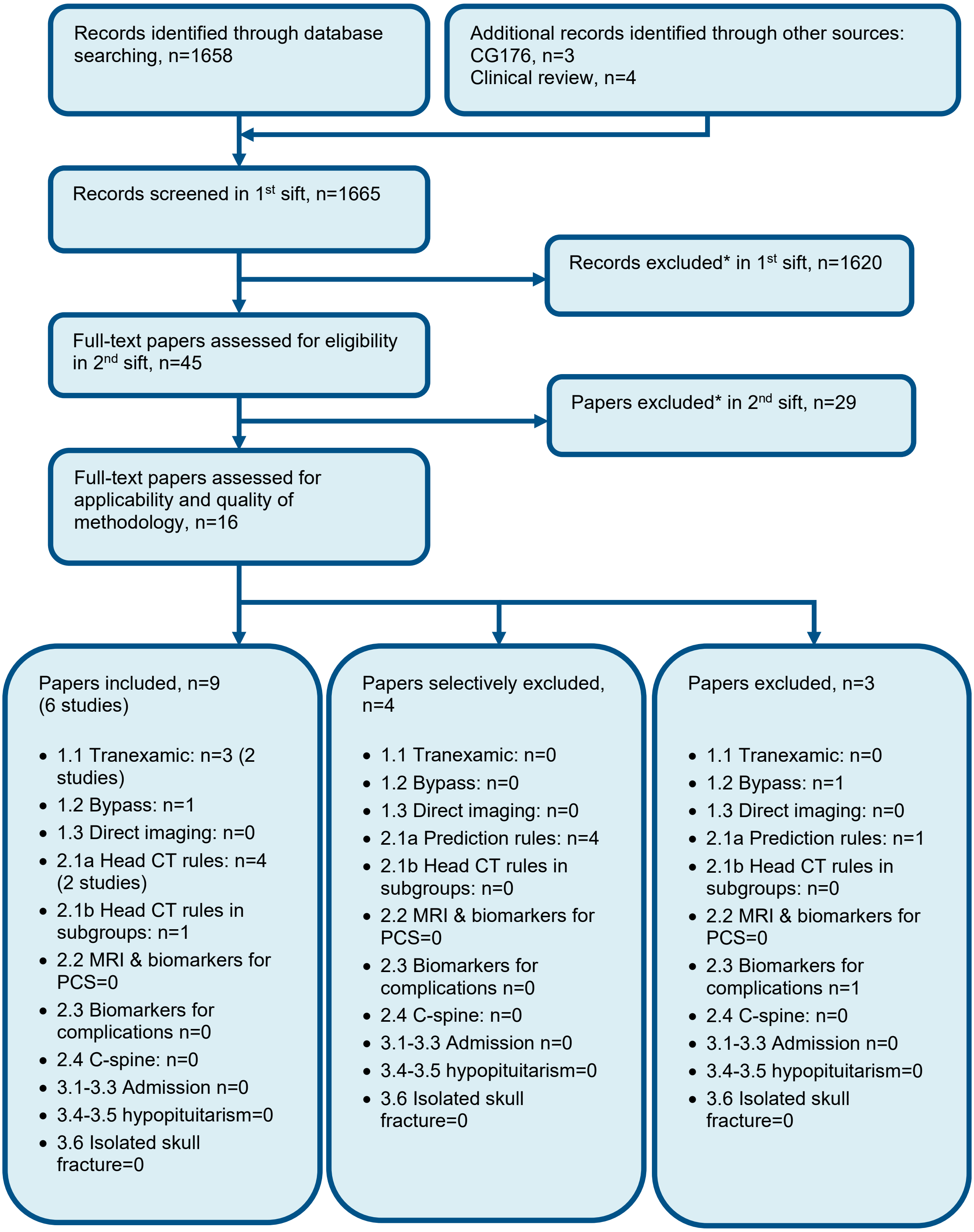
Appendix F – GRADE tables

Table 8: Clinical evidence profile: Linear fracture vs linear fracture + intra cranial lesion – adults and children

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	linear fracture	linear fracture+intra cranial lesion	Relative (95% CI)	Absolute (95% CI)		
Neurosurgical intervention												
1	Case series	serious[a]	not serious	serious[b]	not serious	none	0/152 (0.0%)	23/92 (25.0%)	**OR 0.05** (0.02 to 0.13)	**250 fewer per 1,000** (from 338 fewer to 161 fewer)[c]	⨁◯◯◯ Very low	CRITICAL

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias. Risk of bias assessed using Institute of Health Economics (IHE) checklist for case series
b. Downgraded by 1 increment for indirectness. Includes both adults and children
c. Zero events in one arm. Peto odds ratio for forest plot analysis and risk difference for absolute measure.

Appendix G – Economic evidence study selection



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

Appendix H – Economic evidence tables

None.

Appendix I – Economic model

Model specification

Population: People with isolated skull fracture and no other indication for admission. All the clinical studies except one were in infants and children – see 1.1.4. In the base case analysis of the model, the age at time of injury was 2 years and ¾ of patients were male. In sensitivity analyses we looked at ages 18 years and 40 years.

Comparison: Admission for observation vs No admission

Outcomes: NHS cost, Quality-adjusted life-years (QALYs), Cost per QALY gained

Model inputs and methods

Model approach

The cost of the admission was attributed to all patients in the 'Admission' model arm. The proportion of patients that deteriorate requiring neurosurgery was taken from the guideline review. A treatment effect in terms of change in Glasgow Outcome Scale was applied only to the patients that deteriorate. Health state costs and utilities were applied to these patients. For all other patients, health state costs and utilities were not estimated, on the assumption that they would be the same in each arm.

Incidence of deterioration

The proportion of patients with isolated skull fracture that deteriorate after head injury was estimated from the guideline review – see 1.1.6:

- In the base case analysis, we used the estimate of based on the number of people reported to have deteriorated based on repeat CT scanning. This was 0.24% (0.00%, 0.88%)
- In a sensitivity analysis, we used the estimate of 0.045% (1/2234) based on the number needing neurosurgery in the review.

Treatment effects in the event of deterioration (6 months after injury)

The benefit of admission in the model was due to earlier neurosurgery for those patients that deteriorate. NHS health technology assessment reports were used to identify treatment effects for Immediate vs delayed neurosurgery in terms of Glasgow Outcome Scale. The following were identified and the extracted outcomes are in Table 9:

- Pandor 2011[26] – NHS HTA evaluating decision rules for Head CT for minor head injury

- For the outcome of immediate surgery, 5 studies were pooled together (n=177, Cheung 2007[5], Cook 1985[6], Gerlach 2009[12], Haselsberger 1988[13], and Lee 1998)[19]. For the treatment effect of immediate surgery versus delayed surgery they seem to have used Deverill 2007[9].
- This has been used in the base case analysis of the guideline economic model.

- Deverill 2007[9] (Cited in Pandor 2011[26])
  - A series of patients requiring surgery for extradural haemorrhage from 10 centres in Queensland, Australia. Forty-six patients underwent interhospital transfer before decompressive craniotomy; their median time interval from presentation to operation was 8 h 5 min. This delay was significantly greater than that for 25 patients admitted directly to neurosurgical centres (median 4 h 19).
- Haselsberger 1988[13] (Cited in Pandor 2011[26])
  - A series of 171 patients suffering acute subdural haemorrhage or epidural haemorrhage after closed head injury at the University Hospital of Graz in Austria. They compared timing of surgery - <2 hours vs >2 hours from injury.
- Lecky 2016[18] – NHS HTA feasibility study investigating transportation straight to neurosurgery.
  - For secondary transfer they used the outcomes for 87 patients in the Nottingham Head Injury Register (Fuller 2011[11]) with moderate or severe TBI who were transferred to the Queen's Medical Centre for neurosurgery. For the treatment effect a proportional odds ratio for an unfavourable outcome (GOS<4) of 0.53 was applied based on expert opinion.

Table 9: Glasgow outcome scale for immediate neurosurgery compared to delayed neurosurgery

	Pandor 2011[26] (Base case)			Deverill 2007[26]			Haselsberger 1988[13]			Lecky 2016[18]			Smits 2010[31]		
	Immed	Delay	Diff	Immed	Delay	Diff	Immed	Delay	Diff	Immed	Delay	Diff	Immed	Delay	Diff
Good recovery	81%	57%	24%	70%	68%	1%	33%	7%	27%	32%	23%	9%	63%	39%	24%
Moderate disability	9%	7%	3%	22%	11%	10%	33%	7%	27%	30%	22%	8%	31%	22%	9%
Severe disability	3%	12%	-9%	9%	9%	0%	17%	27%	-10%	9%	13%	-4%	0%	10%	-10%
Vegetative state	3%	10%	-7%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Dead	4%	14%	-11%	0%	11%	-11%	17%	60%	-43%	29%	41%	-12%	6%	29%	-23%
	100%	100%		100%	100%		100%	100%		100%	100%		100%	100%	

- Smits 2010[31]
    - 92 patients with a lesion on CT after minor head injury and GOS data at >1 year from the CHIP (CT in Head Injury Patients) multicentre study (Smits 2008[32]). Outcomes for missed lesions were from Cordobes 1981[7] –41 patients with epidural haematoma before the advent of CT.

Longer-term survival after neurosurgery

The Multi-Society Task Force on Persistent Vegetative State reported the mean length of survival for adults and children in a vegetative state as 3.6 and 7.4 years, respectively (stated in Pandor 2011[26]).

For other patients, in the base case analysis, survival was assumed to be the same as the general population. Age-specific annual mortality rates were used to estimate life expectancy using ONS lifetables for England 2017-19[25]. In a sensitivity analysis a standardised mortality ratio of 2.2 was applied over the lifetime based on a chort of people in Glasgow with head injury, which was followed up fror 13 years.[21]

Intervention cost

The cost of the admission for observation (£521) was assumed to be a short stay from NHS reference costs 2019/20[24] - see 1.1.10. Neurosurgery was not costed as this was assumed to be the same in both model arms.

Utilities (quality of life scores) and Costs by GOS state

These were assumed to be the same as for the guideline model evaluating tranexamic acid (See Evidence Report A and Full model report appendix).

Table 10: NHS costs and utilities by Glasgow Outcome Scale state

	Cost – first year[2, 10]	Cost - subsequent years[2, 10]	Utility[34]
Good recovery	£313	£28	0.894*
Moderate disability	£22,361	£1,843	0.675
Severe disability	£44,176	£14,404	0.382
Vegetative state	£109,475	£109,475	-0.178
Dead	£0	£0	0

** In the good recovery state age/sex-specific utilities were used after 12 years using data from the Health Survey for England.[16]*

Intermediate results

Table 11 shows the change in outcomes as a result of earlier surgery for each patient that deteriorates. These figures are crucial because if early surgery is not cost effective then admission cannot be cost effective regardless of the risk of deterioration. In all but one scenario immediate surgery was dominant, that is it both increased QALYs and reduced NHS costs. These figures are then combined with the cost of an admission and the incidence of deterioration to estimate the mean outcomes for Admission vs No Admission.

Table 11: Impact of Immediate surgery for patients that deteriorate

Analysis	Cost		QALY		Deteriorating patients	
	Immediate	Delayed	Immediate	Delayed	Incr Cost	Incr QALYs
Base case (probabilistic)	£40,247	£127,276	21.84	16.35	-£87,029	5.49
Base case (deterministic)	£40,295	£127,104	21.84	16.36	-£86,809	5.49
Effect size						
Effects from Deverill 2007	£52,865	£48,519	21.94	19.73	£4,346	2.21
Effects from Haselsberger 1988	£96,365	£124,349	16.05	5.72	-£27,984	10.33
Effects from Lecky 2016	£63,903	£75,414	14.26	11.08	-£11,511	3.18
Effects from Smits 2010	£23,236	£61,457	21.14	14.67	-£38,222	6.47
Age						
Age=18 years	£26,404	£81,024	14.37	10.78	-£54,619	3.59
Age=40 years	£24,956	£76,889	12.30	9.24	-£51,933	3.06
Other						
SMR of 2.2 applied to mortality	£39,785	£125,648	21.27	15.93	-£85,863	5.35
Utilities from Smits 2010 but VS state utility equals base case value	£40,295	£127,104	21.10	15.20	-£86,809	5.90

For main results, see main text (1.1.9).

The parameters used in the base case analysis are listed in Table 12 with the distributions used in the probabilistic analysis.

Table 12: Overview of parameters and parameter distributions used in the base case model

Input	Data	Source	Probability distribution
Perspective	UK NHS & personal social services	NICE reference case[23]	n/a
Time horizon	Lifetime	NICE reference case[23]	n/a
Discount rate	Costs: 3.5% Outcomes: 3.5%	NICE reference case[23]	n/a
Cohort settings			
Cohort starting age	2 years	Assumed	n/a
Percentage male	75%	Assumed	n/a
Risk of deterioration			
Delayed intracranial haematoma on CT	0.24%	Guideline review (See 1.1.6)	Beta Alpha=1 Beta=2233
Glasgow outcome scale at 6 months			
Immediate Good recovery Moderate disability Severe disability Vegetative state Dead	 80.5% 9.0% 2.1% 2.4% 6.1%	Pandor 2011[27]	Dirichlet 132 15 3 4 10
Delayed Good recovery Moderate disability Severe disability Vegetative state Dead	 62.5% 4.9% 12.7% 5.8% 14.1%		Dirichlet 24 2 5 2 6
Mortality – see Economic analysis report on Tranexamic acid			
Vegetative state (VS) per year	13%	Derived from Pandor 2011[27] – Life expectancy = 7.4 years for children	n/a
From 6 months to 1 year (not VS)	1.7%	Derived from Severe traumatic brain injury cohort of Whitnall 2006[35]	Beta Alpha=12, Beta=73 Then converted to a rate from a 5-year probability.
Mortality beyond 1 year, per year (not VS)	National Life Tables 2017 - 2019	Office for National Statistics[25]	n/a
Health-related quality of life (utilities) – see Economic analysis report on Tranexamic acid			
Full health	1.000	By definition	n/a
Good recovery	0.894	Fuller 2017[34]	Gamma for decrement vs full health Alpha=575, Beta=0.00

Input	Data	Source	Probability distribution
Moderate disability	0.675	Fuller 2017[34]	Gamma for decrement vs GR Alpha=605, Beta=0.00
Severe disability	0.382	Fuller 2017[34]	Gamma for decrement vs MD Alpha=439, Beta=0.00
Vegetative state	-0.178	Fuller 2017[34]	Gamma for decrement vs SD Alpha=51, Beta=0.01
Dead	0.000	By definition	n/a
Costs			
Intervention costs			
Admission	£521	Estimated based on data from NHS reference costs 2017/18[8] and NHS reference costs 2019/20[24]	Gamma Alpha=25, Beta=21
Post-discharge costs – see Economic analysis report on Tranexamic acid			
First year – Good recovery	£313	Reported in Williams 2020[36], derived from Beecham 2009[3]	Gamma Alpha=25, Beta=13
First year – Moderate disability	£22,361	Williams 2020[36], derived from Beecham 2009[3]	Gamma Alpha=25, Beta=894
First year – Severe disability	£44,176	Williams 2020[36], derived from Beecham 2009[3]	Gamma Alpha=25, Beta=1767
Subsequent years – Good recovery	£28	Williams 2020[36]	Gamma Alpha=25, Beta=1
Subsequent years – Moderate disability	£1,843	Williams 2020[36]	Gamma Alpha=25, Beta=74
Subsequent years – Severe disability	£14,404	Williams 2020[36]	Gamma Alpha=25, Beta=576
Vegetative state (first and subsequent years)	£109,475	Formby 2015[10]	Gamma Alpha=25, Beta=4379

Appendix J – Excluded studies

Clinical studies

Table 13: Studies excluded from the clinical review

Study	Code [Reason]
Adepoju, Adedamola and Adamo, Matthew A (2017) Posttraumatic complications in pediatric skull fracture: dural sinus thrombosis, arterial dissection, and cerebrospinal fluid leakage. Journal of neurosurgery. Pediatrics 20(6): 598-603	- Population not relevant to this review protocol *Includes mixed severity. Mild, moderate and severe TBI.*
Adetayo, Oluwaseun A, Naran, Sanjay, Bonfield, Christopher M et al. (2015) Pediatric Cranial Vault Fractures: Analysis of Demographics, Injury Patterns, and Factors Predictive of Mortality. The Journal of craniofacial surgery 26(6): 1840-6	- Population not relevant to this review protocol *children with severe TBI*
Asirdizer, Mahmut, Kartal, Erhan, Ekiz, Aykut et al. (2021) The effect of the presence or absence of skull fractures on intracranial lesion development in road traffic accidents. Journal of forensic and legal medicine 84: 102269	- Population not relevant to this review protocol *Participants with depressed or open fractures*
Bonfield, Christopher M, Naran, Sanjay, Adetayo, Oluwaseun A et al. (2014) Pediatric skull fractures: the need for surgical intervention, characteristics, complications, and outcomes. Journal of neurosurgery. Pediatrics 14(2): 205-11	- Full text paper not available
Bressan S, Marchetto L, Lyons TW et al. (2018) A Systematic Review and Meta-Analysis of the Management and Outcomes of Isolated Skull Fractures in Children. Annals of emergency medicine 71(6): 714-724.e2	- Systematic review used as source of primary studies *Does not include all protocol outcomes*
Brown, Craig W; Akbar, Sairah P; Cooper, Jamie G (2014) Things that go bump in the day or night: the aetiology of infant head injuries presenting to a Scottish Paediatric Emergency Department. European journal of emergency medicine : official journal of the European Society for Emergency Medicine 21(6): 447-50	- Population not relevant to this review protocol *only 3 participants with isolated skull fracture. Results not reported separately for this group.*
Chan, K H, Mann, K S, Yue, C P et al. (1990) The significance of skull fracture in acute traumatic intracranial hematomas in adolescents: a prospective study. Journal of neurosurgery 72(2): 189-94	- No protocol outcomes

Study	Code [Reason]
Donaldson, Katelyn, Li, Xun, Sartorelli, Kennith H et al. (2019) Management of Isolated Skull Fractures in Pediatric Patients: A Systematic Review. Pediatric emergency care 35(4): 301-308	- Systematic review used as source of primary studies
Erlichman, David B, Blumfield, Einat, Rajpathak, Swapnil et al. (2010) Association between linear skull fractures and intracranial hemorrhage in children with minor head trauma. Pediatric radiology 40(8): 1375-9	- Study design not relevant to this review protocol *case control study*
Fujiwara, Gaku, Okada, Yohei, Ishii, Wataru et al. (2021) Association of skull fracture with in-hospital mortality in severe traumatic brain injury patients. The American journal of emergency medicine 46: 78-83	- Population not relevant to this review protocol *people with severe TBI*
Gardner, James E; Teramoto, Masaru; Hansen, Colby (2019) Factors Associated With Degree and Length of Recovery in Children With Mild and Complicated Mild Traumatic Brain Injury. Neurosurgery 85(5): e842-e850	- Study design not relevant to this review protocol *survey*
Ghani, F.; Siddiq, M.; Idrees, M. (2018) Frequency of extradural hematoma among patients presenting with traumatic brain injury with skull fracture. Journal of Medical Sciences (Peshawar) 26(3): 242-245	- No protocol outcomes
Greenes, D S and Schutzman, S A (1999) Clinical indicators of intracranial injury in head-injured infants. Pediatrics 104(4pt1): 861-7	- Not all had CT *head and/or skull x-ray*
Greenes, D S and Schutzman, S A (1997) Infants with isolated skull fracture: what are their clinical characteristics, and do they require hospitalization?. Annals of emergency medicine 30(3): 253-9	- Not all had CT *Not all had CT. Children had either skull x-ray, ultrasound or CT*
Joseph, Bellal, Pandit, Viraj, Aziz, Hassan et al. (2015) Mild traumatic brain injury defined by Glasgow Coma Scale: Is it really mild?. Brain injury 29(1): 11-6	- Mixed population. results not reported separately for isolated skull fracture
Katirci, Y., Ocak, T., Karamercan, M.A. et al. (2013) Compliance with catch rules in administering computerized tomography scans to children admitted to the emergency department with minor head trauma. Acta Medica Mediterranea 29(4): 717-722	- Population not relevant to this review protocol *Includes mild, moderate and severe TBI. Includes children with open, depressed or basal skull fractures fractures.*

Study	Code [Reason]
Lefort, Roxanna, Hunter, Jill V, Cruz, Andrea T et al. (2017) Utility of Emergency Department Observation Units for Neurologically Intact Children With Head CT Abnormalities Secondary to Acute Closed Head Injury. Pediatric emergency care 33(3): 161-165	- Mixed population. results not reported separately for isolated skull fracture
Lewis, Paul R, Dunne, Casey E, Wallace, James D et al. (2017) Routine neurosurgical consultation is not necessary in mild blunt traumatic brain injury. The journal of trauma and acute care surgery 82(4): 776-780	- Mixed population. results not reported separately for isolated skull fracture
Lyons TW, Stack AM, Monuteaux MC et al. (2016) A QI Initiative to Reduce Hospitalization for Children With Isolated Skull Fractures. Pediatrics 137(6)	- Not all had CT *Not all had CT. Children had either skull x-ray, CT or MRI*
Maharaj, Prashanth and Enicker, Basil (2022) Compound elevated skull fractures: a retrospective descriptive study. British journal of neurosurgery: 1-6	- results not reported separately for isolated skull fracture *Mixed population.*
Marincowitz, Carl, Lecky, Fiona E, Allgar, Victoria et al. (2020) Development of a Clinical Decision Rule for the Early Safe Discharge of Patients with Mild Traumatic Brain Injury and Findings on Computed Tomography Brain Scan: A Retrospective Cohort Study. Journal of neurotrauma 37(2): 324-333	- Mixed population. *Results not reported separately for simple skull fracture. Study included in small intra cranial injuries review.*
Marincowitz, Carl, Paton, Lewis, Lecky, Fiona et al. (2022) Predicting need for hospital admission in patients with traumatic brain injury or skull fractures identified on CT imaging: a machine learning approach. Emergency medicine journal : EMJ 39(5): 394-401	- Population not relevant to this review protocol *Mixed population (skull fracture+intra cranial injury). Results not reported separately for isolated skull fracture.*
Mogbo, K I, Slovis, T L, Canady, A I et al. (1998) Appropriate imaging in children with skull fractures and suspicion of abuse. Radiology 208(2): 521-4	- Not all had CT
Montoya-Filardi, A, Menor Serrano, F, Llorens Salvador, R et al. (2020) Linear skull fracture in infants after mild traumatic brain injury: influence of computed tomography in management. Radiologia 62(6): 487-492	- Study not reported in English
Munoz-Sanchez, M A, Murillo-Cabezas, F, Cayuela, A et al. (2005) The significance of skull	- No protocol outcomes

Study	Code [Reason]
fracture in mild head trauma differs between children and adults. Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery 21(2): 128-32	
Munoz-Sanchez, M A, Murillo-Cabezas, F, Cayuela-Dominguez, A et al. (2009) Skull fracture, with or without clinical signs, in mTBI is an independent risk marker for neurosurgically relevant intracranial lesion: a cohort study. Brain injury 23(1): 39-44	- Population not relevant to this review protocol *All participants did not have CT. Either skull x-ray or CT*
Nakahara, Kuniaki, Shimizu, Satoru, Utsuki, Satoshi et al. (2011) Linear fractures occult on skull radiographs: a pitfall at radiological screening for mild head injury. The Journal of trauma 70(1): 180-2	- Not all had CT - Population not relevant to this review protocol *Mixed population (skull fracture+ intra cranial injury). Results not reported separately for isolated skull fracture.*
Noje, Corina, Jackson, Eric M, Nasr, Isam W et al. (2019) Trauma Bay Disposition of Infants and Young Children With Mild Traumatic Brain Injury and Positive Head Imaging. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies 20(11): 1061-1068	- Mixed population. results not reported separately for isolated skull fracture
Northam, W., Chandran, A., Quinsey, C. et al. (2019) Pediatric nonoperative skull fractures: Delayed complications and factors associated with clinic and imaging utilization. Journal of Neurosurgery: Pediatrics 24(5): 489-497	- Full text paper not available
Plackett, Timothy P, Asturias, Sabrina, Tadlock, Matthew et al. (2015) Re-evaluating the need for hospital admission and observation of pediatric traumatic brain injury after a normal head CT. Journal of pediatric surgery 50(10): 1758-61	- Population not relevant to this review protocol *Includes mild, moderate and severe TBI. Results not reported separately for children with non-displaced skull fracture.*
Powell, Elizabeth C, Atabaki, Shireen M, Wootton-Gorges, Sandra et al. (2015) Isolated linear skull fractures in children with blunt head trauma. Pediatrics 135(4): e851-7	- Not all had CT *Not all had CT. Either skull x-ray and CT*
Sadasivam, S. (2016) Pattern of cranio cerebral injuries in fatal cases of road traffic accidents. Medico-Legal Update 16(2): 173-177	- No protocol outcomes

Study	Code [Reason]
Schunk JE; Rodgerson JD; Woodward GA (1996) The utility of head computed tomographic scanning in pediatric patients with normal neurologic examination in the emergency department. Pediatric emergency care 12(3): 160-165	- Population not relevant to this review protocol *Mixed population (skull fracture+ intra cranial injury). Includes linear, depressed, basilar skull fractures. Results not reported separately for isolated skull fracture.*
Servadei, F, Ciucci, G, Morichetti, A et al. (1988) Skull fracture as a factor of increased risk in minor head injuries. Indication for a broader use of cerebral computed tomography scanning. Surgical neurology 30(5): 364-9	- Population not relevant to this review protocol *All participants did not have CT. Either skull x-ray or CT*
Servadei, F, Ciucci, G, Pagano, F et al. (1988) Skull fracture as a risk factor of intracranial complications in minor head injuries: a prospective CT study in a series of 98 adult patients. Journal of neurology, neurosurgery, and psychiatry 51(4): 526-8	- Population not relevant to this review protocol *All participants did not have CT. Either skull x-ray or CT*
Singata, Chuma and Candy, Sally (2018) Is computed tomography of the head justified in patients with minor head trauma presenting with Glasgow Coma Scale 15/15?. SA journal of radiology 22(1): 1329	- results not reported separately for isolated skull fracture
Tallapragada, Krishna; Peddada, Ratna Soundarya; Dexter, Mark (2018) Paediatric mild head injury: is routine admission to a tertiary trauma hospital necessary?. ANZ journal of surgery 88(3): 202-206	- Mixed population. results not reported separately for isolated skull fracture
Trenchs, Victoria, Curcoy, Ana I, Castillo, Marta et al. (2009) Minor head trauma and linear skull fracture in infants: cranial ultrasound or computed tomography?. European journal of emergency medicine : official journal of the European Society for Emergency Medicine 16(3): 150-2	- Not all had CT *Not all had CT. Children had either skull x-ray, ultrasound or CT*
Tseng, Wei-Chun, Shih, Hong-Mo, Su, Yi-Chun et al. (2011) The association between skull bone fractures and outcomes in patients with severe traumatic brain injury. The Journal of trauma 71(6): 1611-1614	- Population not relevant to this review protocol *People with severe TBI*
White, Ian K, Pestereva, Ecaterina, Shaikh, Kashif A et al. (2016) Transfer of children with isolated linear skull fractures: is it worth the cost?. Journal of neurosurgery. Pediatrics 17(5): 602-6	- Full text paper not available

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2005 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.